FIGURE 1A

102

A(n)

103

A(n)

104

A(n)

105

A(n)

106

A(n)

FIGURE 1B-1

107

A(n)

108

M1   A(n) 191

M2   A(n) 192

M3   A(n) 193

109

NS1   A(n) 194

NS2   A(n) 195

FIGURE 1B-2

FIGURE 2

320
(2nt 3' overhang)

sense (310)

OH

P   P

HO   antisense
                                                          (315)

320 (2nt 3'   300
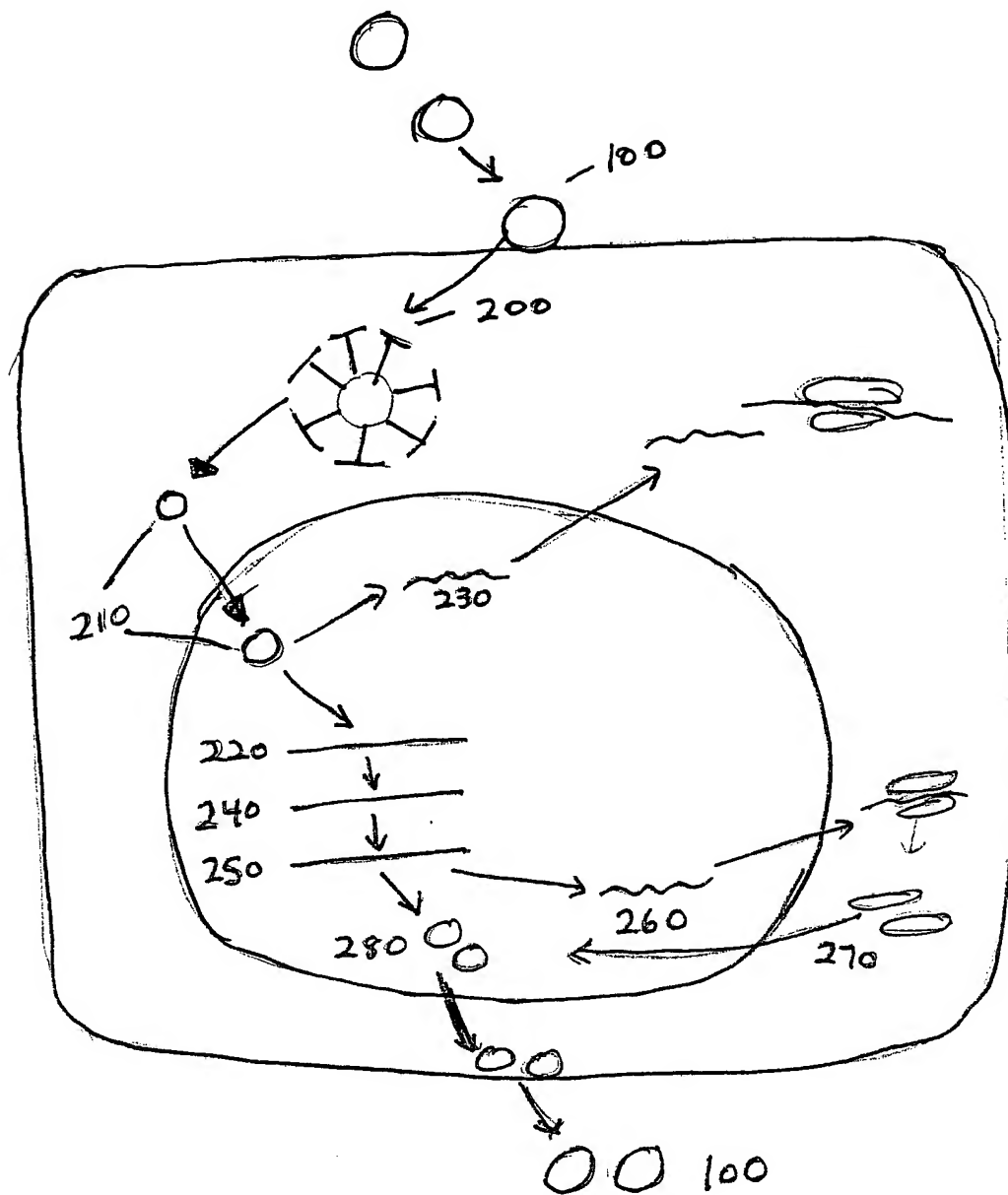overhang)

DS portion
(core region)

FIGURE 3

RNAi in Drosophila

long dsRNA

siRNA

↓

$m7G(5')ppp(5')G$

AAAA mRNA

↓ Helicase?

↓ slicing of mRNA by RISC Complex
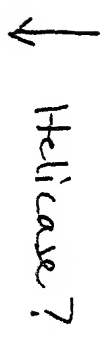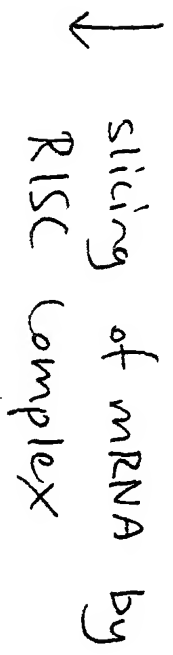
$m7G(5')ppp(5')G$

AAAA mRNA

↓

transcript degradation

FIGURE 4

A

HO —||||||||||||||||||||||||||— P
   330   300   P
)‾‾‾( )‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾(

P —||||||||||||||||||||||||||— OH
   330   300   320
)‾‾‾‾‾‾‾‾‾‾‾( )‾‾(

B

HO —|||||||||||||||||||||⟨◯⟩
   330   410
)‾‾‾( )‾‾‾‾‾‾‾‾‾‾‾( )‾‾(
                        410

C

⟨◯⟩——|||||||||||||||||||||⟨◯⟩
   410   400   410
)‾‾‾( )‾‾‾‾‾‾‾‾‾‾‾‾‾( )‾‾(

FIGURE 5

2-3nt mismatches

Target
Transcript

3'UTR

X Translation

AAAA

FIGURE 6

P1 t_2

~19 nt

t_1 P2

transcript 1

+

transcript 2

HO
3'

3'
OH

FIGURE 7

Promoter

1st complementary region

2nd complementary region

Terminator

Optional loop

HO –

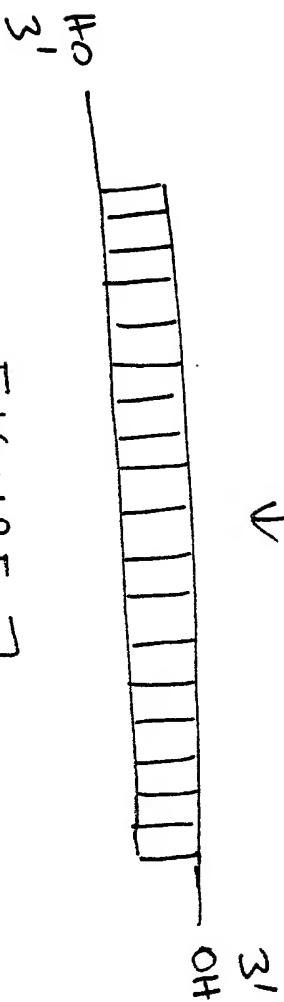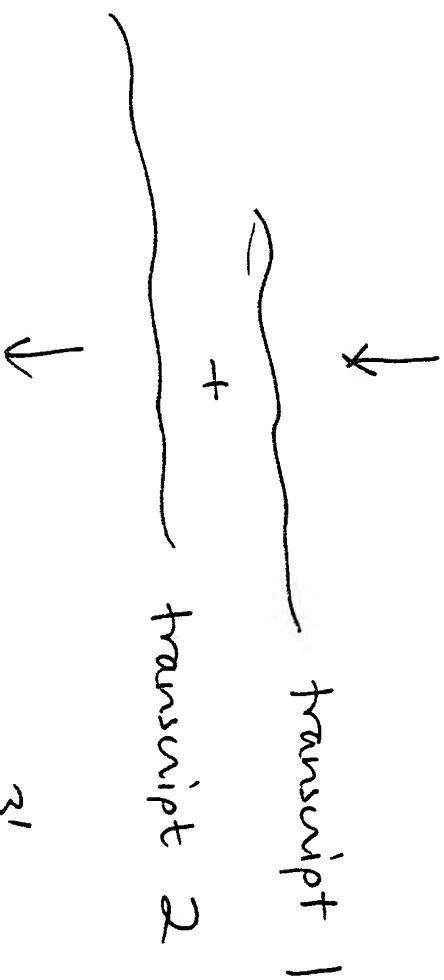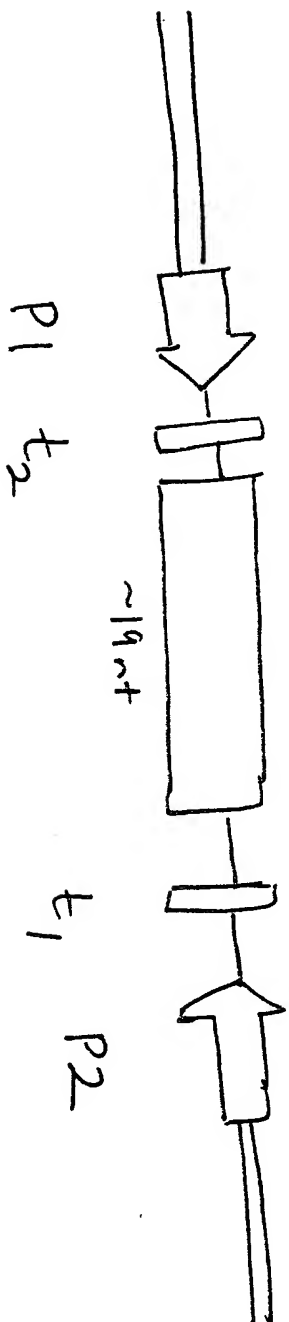3' –
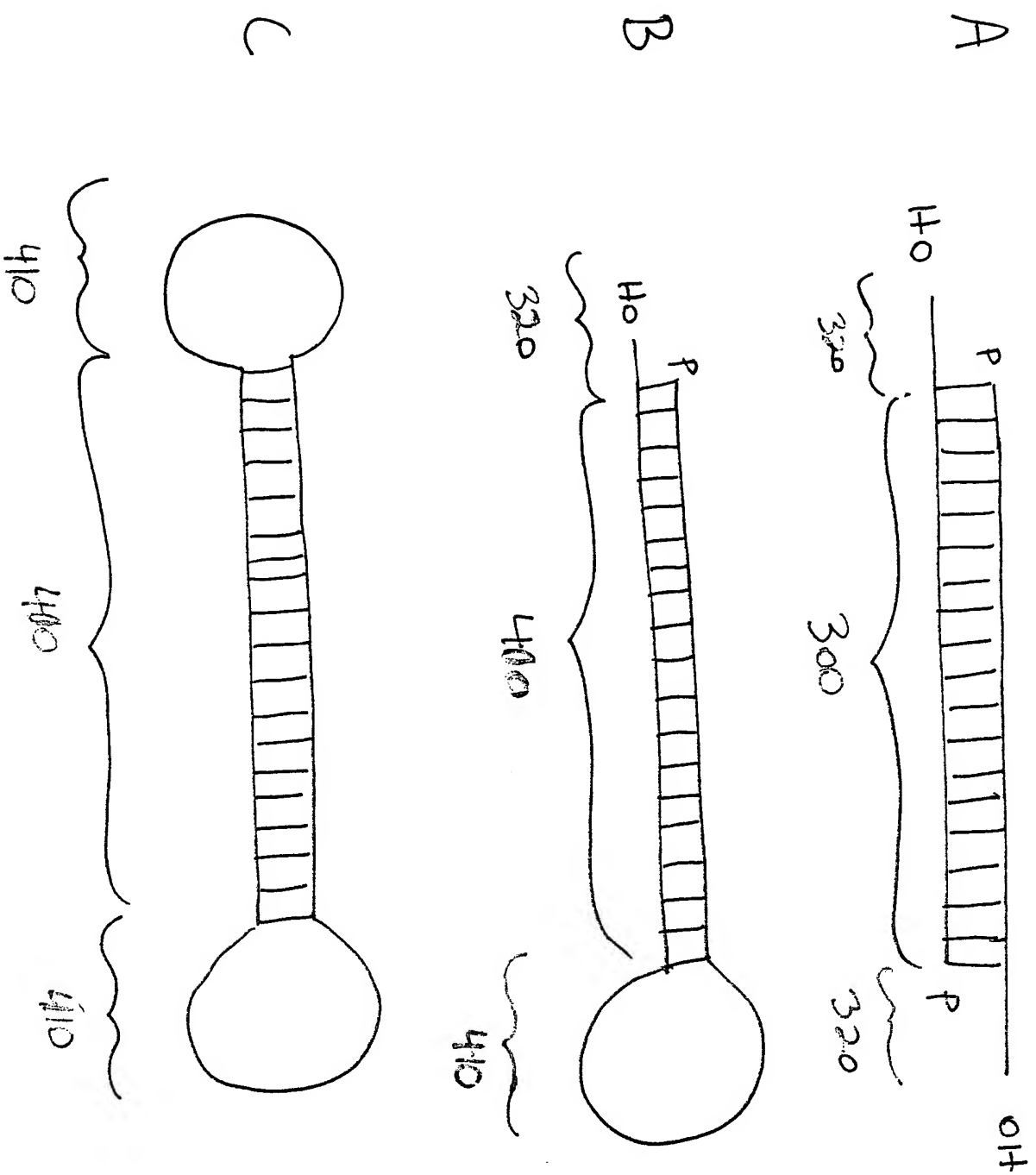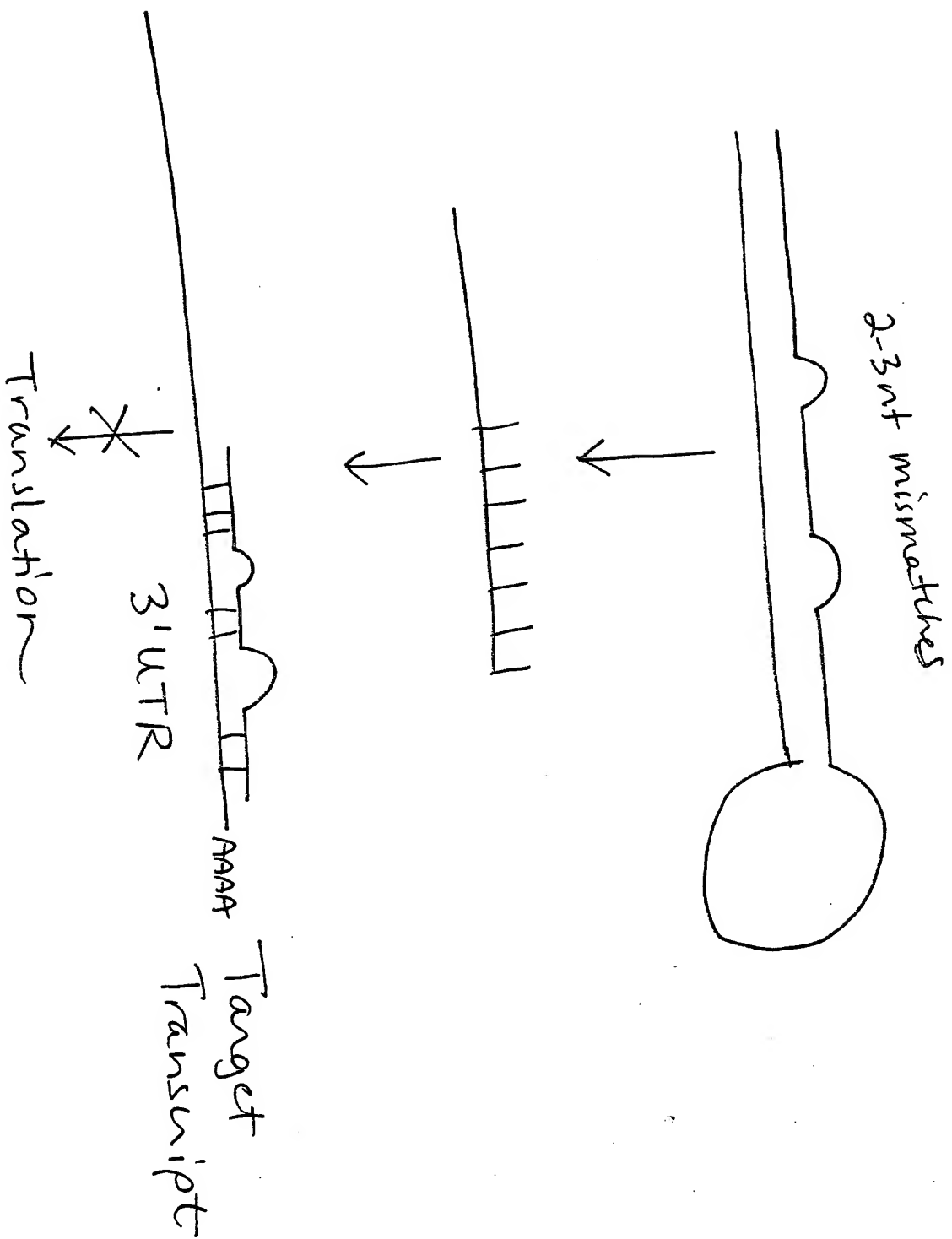
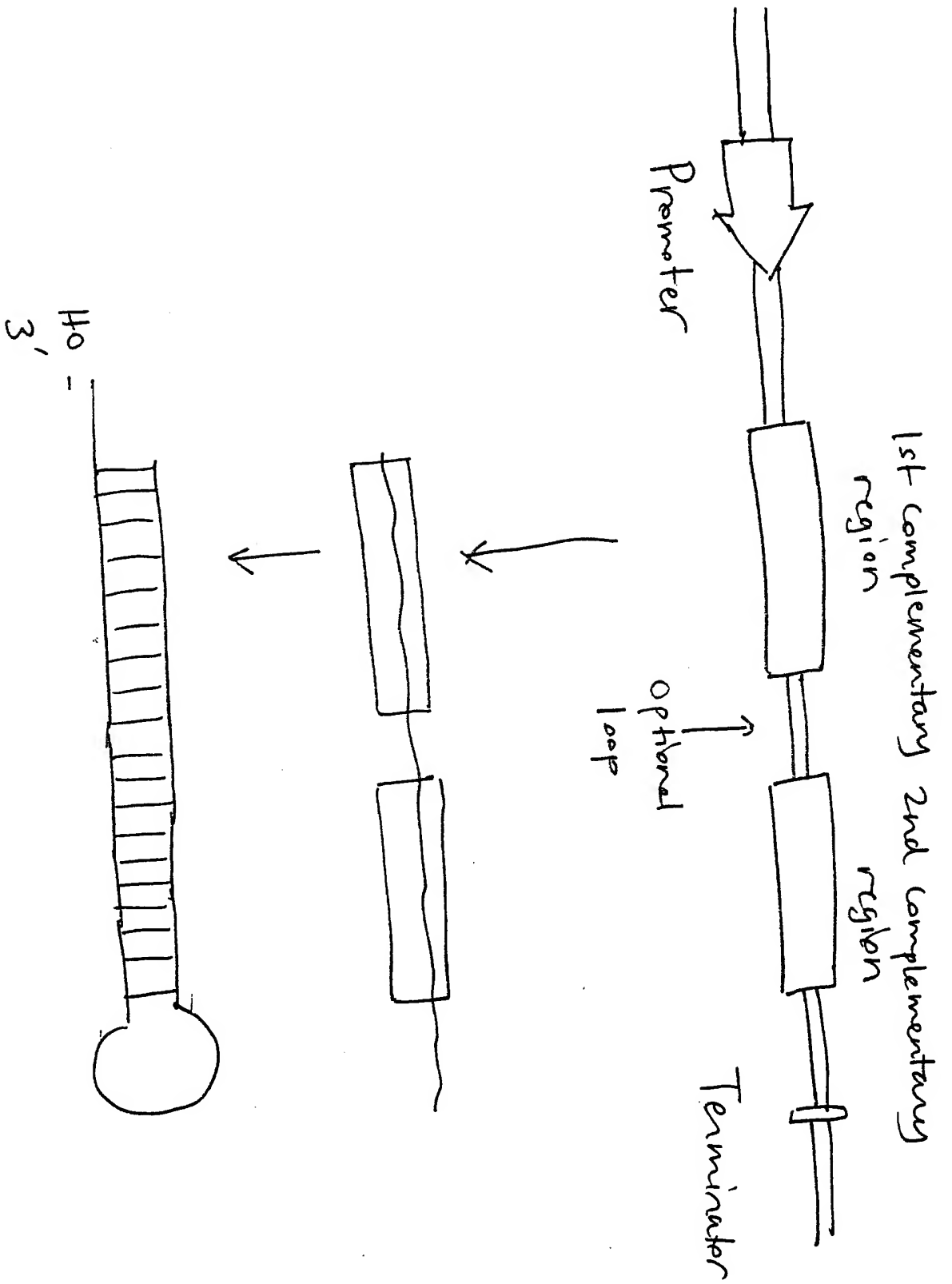FIGURE 8

Figure 9

CLUSTAL W(1.4) multiple sequence alignment

Shaded area: Highly conserved regions selected as siRNA sequences.

Genbank Acc. No.	Strain			Length
NC_002022	A/Puerto Rico/8/34	H1N1	1934	2233 nt
X17336	A/WSN/33	H1N1	1933	2233 nt
M81579	A/Leningrad/134/17/57	H2N2	1957	2233 nt
AF348174	A/Hong Kong/1/68	H3N2	1968	2209 nt
AF257193	A/Hong Kong/481/97	H5N1	1997	2233 nt
AF257191	A/Hong Kong/1073/99	H9N2	1999	2233 nt


```
NC_002022/-    AGCGAAAGCAGGTACTGATCCAAAATGGAAGATTTTGTGCGACAATGCTT
X17336/-       AGCGAAAGCAGGTACTGATTCAAAATGGAAGATTTTGTGCGACAATGCTT
M81579/-       AGCAAAAGCAGGTACTGATCCGAAATGGAAGAATTTGTGCGACAATGCTT
AF348174/-     -------------------------ATGGAAGATTTTGTACGACAATGCTT
AF257193/-     AGCAAAAGCAGGTACTGATCCAAAATGGAAGACTTTGTGCGACAATGCTT
AF257191/-     AGCAAAAGCAGGTACTGATCCGAAATGGAAGACTTTGTGCGACAATGCTT


NC_002022/-    CAATCCGATGATTGTCGAGCTTGCGGAAAAAACAATGAAAGAGTATGGGG
X17336/-       CAATCCGATGATTGTCGAGCTTGCGGAAAAGGCAATGAAAGAGTATGGAG
M81579/-       CAATCCGATGATTGTCGAGCTTGCTGAAAAAGCAATGAAAGAGTATGGAG
AF348174/-     TAATCCGATGATTGTCGAACTTGCGGAAAAGGCAATGAAAGAGTATGGAG
AF257193/-     CAATCCAATGATTGTCGAGCTTGCGGAAAAGACAATGAAGGAGTATGGGG
AF257191/-     CAATCCAATGATTGTCGAGCTTGCGGAAAAGACAATGAAGGAATATGGGG


NC_002022/-    AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
X17336/-       AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
M81579/-       AGGATCGGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
AF348174/-     AGGATCTTAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
AF257193/-     AAGATCCGAAGATTGAAACAAACAAGTTCGCTGCAATATGCACACACTTA
AF257191/-     AAGACCCGAAAATTGAAACAAATAAGTTCGCTGCAATATGCACACACTTA


NC_002022/-    GAAGTATGCTTCATGTATTCAGATTTCCACTTCATCAATGAGCAAGGCGA
X17336/-       GAAGTGTGCTTCATGTATTCAGATTTTCACTTCATCGATGAGCAAGGCGA
M81579/-       GAAGTATGCTTCATGTATTCAGATTTTCATTTCATCAATGAGCAAGGCGA
AF348174/-     GAAGTATGCTTCATGTATTCAGATTTTCATTTCATCAATGAGCAAGGCGA
AF257193/-     GAAGTCTGCTTCATGTATTCAGACTTCCATTTCATTGACGAACGAGGCGA
AF257191/-     GAAGTCTGCTTCATGTATTCAGACTTCCATTTCATTGACGAACGAGGCGA


NC_002022/-    GTCAATAATCGTAGAACTTGGTGATCCTAATGCACTTTTGAAGCACAGAT
X17336/-       GTCAATAGTCGTAGAACTTGGCGATCCAAATGCACTTTTGAAGCACAGAT
M81579/-       GTCAATAATAGTAGAGCTTGATGATCCAAATGCACTTTTGAAGCACAGAT
AF348174/-     GTCAATAGTGGTAGAACTTGATGATCCAAATGCACTTTTGAAGCACAGAT
AF257193/-     ATCAATAATTGTGGAATCTGGTGATCCGAATGCATTGTTGAAACACCGGT
AF257191/-     ATCAATAATTGTGGAATCTGGTGATCCAAATGCATTGTTGAAGCACAGGT


NC_002022/-    TTGAAATAATCGAGGGAAGAGATCGCACAATGGCCTGGACAGTAGTAAAC
X17336/-       TTGAAATAATCGAGGGAAGAGATCGCACAATAGCCTGGACAGTAATAAAC
M81579/-       TTGAAATAATAGAGGGAAGAGATCGCACAATGGCCTGGACAGTAGTAAAC
AF348174/-     TTGAAATAATAGAGGGAAGAGACCGCACAATGGCCTGGACAGTAGTAAAC
AF257193/-     TTGAAATAATTGAAGGAAGAGACCGAGCAATGGCCTGGACAGTGGTGAAT
AF257191/-     TTGAAATAATTGAAGGAAGAGACCGAGCAATGGCCTGGACAGTGGTGAAT


NC_002022/-    AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
X17336/-       AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
M81579/-       AGTATTTGCAACACTACAGGAGCTGAGAAACCGAAGTTTCTGCCAGATTT
AF348174/-     AGTATTTGCAACACCACAGGAGCTGAGAAACCGAAGTTTCTGCCAGATTT
AF257193/-     AGCATCTGCAACACCACAGGAGTCGATAAACCCAAATTTCTTCCGGATCT
AF257191/-     AGCATCTGCAACACAACAGGAGTCGATAAACCCAAATTTCTTCCGGATCT
```

Figure 9

```
NC_002022/-    GTATGATTACAAGGAAAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
X17336/-       GTATGATTACAAGAAGAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
M81579/-       GTATGATTACAAGGAGAATAGATTCATCGAGATTGGAGTGACAAGGAGGG
AF348174/-     GTATGATTACAAGGAGAATAGATTCATCGAGATTGGAGTGACAAGGAGAG
AF257193/-     ATACGACTACAAGGAAAACCGATTCACTGAAATTGGTGTGACACGGAGGG
AF257191/-     ATACGACTACAAGGAAAACCGATTCACTGAAATTGGTGTGACACGGAGGG


NC_002022/-    AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAA
X17336/-       AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAG
M81579/-       AAGTCCACATATACTATCTTGAAAAGGCCAATAAAATTAAATCTGAGAAG
AF348174/-     AAGTCCACATATACTACCTTGAAAAGGCCAATAAAATTAAATCTGAGAAT
AF257193/-     AAGTTCATATATATTACTTAGAGAAAGCTAACAAGATAAAATCCGAGAAA
AF257191/-     AAGTTCACATATATTACTTAGAAAAAGCTAACAAGATAAAATCCGAGAAA


NC_002022/-    ACACACATCCACATTTTCTCGTTCACTGGGGAAGAAATGGCCACAAAGGC
X17336/-       ACACACATCCACATTTTCTCATTCACTGGGGAGGAAATGGCCACAAAGGC
M81579/-       ACACACATCCACATTTTCTCATTCACTGGGGAAGAAATGGCCACAAAGGC
AF348174/-     ACACACATCCACATTTTCTCATTCACTGGGGAAGAAATGGCCACAAAGGC
AF257193/-     ACACATATCCACATCTTCTCATTCACTGGAGAAGAAATGGCCACTAAAGC
AF257191/-     ACACATATCCACATCTTTTCATTCACTGGAGAAGAAATGGCCACTAAAGC


NC_002022/-    CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
X17336/-       CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
M81579/-       CGACTACACTCTCGATGAGGAAAGCAGGGCTAGGATCAAGACCAGACTAT
AF348174/-     CGACTACACTCTCGATGAGGAAAGCAGGGCTAGGATCAAAACCAGACTAT
AF257193/-     TGACTACACCCTTGATGAAGAGAGCAGGGCAAGAATCAAAACCAGACTAT
AF257191/-     TGACTACACCCTTGATGAAGAGAGCAGGGCAAGAATAAAAACCAGACTAT


NC_002022/-    TCACCATAAGACAAGAAATGGCCAGCAGAGGCCTCTGGGATTCCTTTCGT
X17336/-       TCACCATAAGACAAGAAATGGCTAGCAGAGGCCTCTGGGATTCCTTTCGT
M81579/-       TCACCATAAGACAAGAAATGGCTAGCAGAGGCCTCTGGGATTCCTTTCGT
AF348174/-     TCACCATAAGACAAGAGATGGCCAACAGAGGCCTCTGGGATTCCTTTCGT
AF257193/-     TCACCATAAGACAGGAAATGGCAAGCAGGGGTCTATGGGACTCCTTTCGT
AF257191/-     TCACCATAAGACAGGAAATGGCAAGCAGGGGTCTATGGGATTCCTTTCGT


NC_002022/-    CAGTCCGAGAGAGGAGAAGAGACAATTGAAGAAAGGTTTGAAATCACAGG
X17336/-       CAGTCCGAGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M81579/-       CAGTCCGAAAGAGAGGCGAAGAAACAATTGAAGAAAGATTTGAAATCACAGG
AF348174/-     CAGTCCGAAAGAGAGGCGAAGAAACAATTGAAGAAAGATTTGAAATCACAGG
AF257193/-     CAGTCCGAGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
AF257191/-     CAGTCCGAGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG


NC_002022/-    AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCGAACTTCTCCAGCC
X17336/-       AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCAAACTTCTCCAGCC
M81579/-       GACAATGCGCAGGCTCGCCGACCAAAGTCTCCCGCCGAACTTCTCCTGCC
AF348174/-     GACAATGCGCAGGCTTGCCGACCAAAGTCTCCCGCCGAACTTCTCCTGCC
AF257193/-     GACCATGCGTAGGCTTGCCGACCAAAGTCTCCCACCTAACTTCTCCAGCC
AF257191/-     GACCATGCGTAGGCTTGCCGACCAAAGTCTCCCACCTAACTTCTCCAGCC


NC_002022/-    TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
X17336/-       TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCCAACGGCTACATT
M81579/-       TTGAGAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
AF348174/-     TTGAGAATTTTAGAGCCTATGTGGATGGATTTAAACCGAACGGCTGCATT
AF257193/-     TTGAAAACTTTAGAGCCTATGTGGATGGATTTAAACCGAACGGCTGCATT
AF257191/-     TTGAAAACTTTAGAGCCTATGTGGATGGATTCAAACCGAACGGCTGCATT


NC_002022/-    GAGGGCAAGCTGTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
```

Figure 9

```
X17336/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
M81579/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCTAAAATTGAGCC
AF348174/-    GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTGAATGCAAAAATTGAACC
AF257193/-    GAGGGCAAGCTTTCTCAAATGTCGAAAGAAGTGAAGCCAGAATTGAGCC
AF257191/-    GAGGGCAAGCTTTCTCAAATGTCGAAAGAAGTGAACGCCAGAATTGAGCC


NC_002022/-   TTTTTTGAAAACAACACCACGACCACTTAGACTTCCGAATGGGCCTCCCT
X17336/-      TTTTTTGAAAACAACACCACGACCACTTAGACTTCCGGATGGGCCTCCCT
M81579/-      TTTTCTGAAAACAACACCAAGACCAATTAGACTTCCGGATGGGCCTCCTT
AF348174/-    TTTTCTGAAAACAACACCAAGACCAATTAGACTTCCGGATGGGCCTCCTT
AF257193/-    ATTTCTGAAGACAACACCACGTCCTCTCAGATTGCCTGATGGACCTCCCT
AF257191/-    ATTTCTGAAGACAACACCACGTCCCCTCAGATTGCCTGATGGACCTCCCT


NC_002022/-   GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
X17336/-      GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
M81579/-      GGTCTCAGCGGTCCAAATTCCTGCTGATGGATGCTTTAAAATTAAGCATT
AF348174/-    GTTTTCAGCGGTCCAAATTCCTTCTGATGGATGCTTTAAAGTTAAGCATT
AF257193/-    GCTCCCAGCGGTCGAAATTCTTGCTGATGGATGCTCTGAAATTAAGCATT
AF257191/-    GCTCCCAGCGGTCGAAATTCTTGCTGATGGATGCTCTGAAATTAAGCATT


NC_002022/-   GAGGACCCAAGTCATGAAGGAGAGGGAATACCGCTATATGATGCAATCAA
X17336/-      GAGGACCCAAGTCATGAGGGAGAGGGGATACCGCTATATGATGCAATCAA
M81579/-      GAGGACCCAAGTCACGAAGGAGAGGGAATACCACTATATGATGCGATCAA
AF348174/-    GAGGATCCAAGTCACGAGGGGGGAGGGAATACCACTATATGATGCGATCAA
AF257193/-    GAGGACCCGAGCCATGAGGGGGGAGGGATACCGCTATATGATGCGATCAA
AF257191/-    GAGGACCCGAGCCATGAGGGGGGAGGGATACCGCTATATGATGCGATAAA


NC_002022/-   ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
X17336/-      ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
M81579/-      GTGTATGAGAACATTCTTTGGATGGAAAGAACCCTATGTTGTTAAACCAC
AF348174/-    ATGCATGAGAACATTTTTTGGATGGAAAGAACCCTATATTGTTAAACCAC
AF257193/-    ATGCATGAAAACATTCTTTGGCTGGAGAGAGCCCAACATCATCAAACCAC
AF257191/-    ATGCATGAAAACATTCTTCGGCTGGAGAGAGCCCAACATCATCAAGCCAC


NC_002022/-   ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
X17336/-      ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
M81579/-      ACGATAAGGGAATAAATCCAAATTATCTGCTGTCATGGAAGCAATTACTG
AF348174/-    ACGAAAAGGGGATAAATCCAAATTATCTGCTGTCATGGAAGCAAGTACTG
AF257193/-    ACGAAAAAGGCATAAATCCAAATTATCTCCTGGCTTGGAAGCAGGTGCTG
AF257191/-    ACGAGAAGGGCATAAATCCCAATTATCTTCTGGCTTGGAAGCAGGTGCTG


NC_002022/-   GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAAGACTAAAAA
X17336/-      GCAGAACTGCAGGACATTGAGAATGAGGAGAAGATTCCAAGAACGAAAAA
M81579/-      GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAGAACTAAAAA
AF348174/-    GCAGAACTGCAGGACATTGAAAATGAGGATAAAATCCCAAAAACAAAGAA
AF257193/-    GCAGAACTCCAGGATATTGAAAATGAGGATAAAATCCCAAAAACAAAGAA
AF257191/-    GCAGAACTCCAGGATATTGAAAATGAGGATAAAATCCCAAAAACAAAGAA


NC_002022/-   TATGAAAAAAACAAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
X17336/-      TATGAAGAAAACGAGTCAGTTAAAGTGGGCACTTGGTGAGAACATGGCAC
M81579/-      CATGAAGAAAACGAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF348174/-    CATGAAGAAAACGAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF257193/-    CATGAAGAAAACAAGCCAATTAATGTGGGCACTCGGAGAGAATATGGCAC
AF257191/-    CATGAAGAAAACAAGCCAATTAATGTGGGCACTCGGGGAGAATATGGCAC


NC_002022/-   CAGAAAAGGTAGACTTTGACGACTGTAAAGATGTAGGTGATTTGAAGCAA
X17336/-      CAGAAAAGGTAGACTTTGACGATGTAAAGATGTAGGCGATTTGAAGCAA
M81579/-      CAGAGAAGGTAGACTTTGACGACTGTAGAGATATAAGCGATTTGAAGCAA
AF348174/-    CAGAGAAGGTAGACTTTGACAACTGTAGAGACGTAAGCGATTTGAAGCAA
```

Figure 9

```
AF257193/-      CGGAAAAAGTGGACTTTGAGGATTGCAAAGACATTGATGATCTGAAACAG
AF257191/-      CGGAAAAATTGGACTTTGAGGACTGCAAAGATATTGGCGATCTGAAACAG


NC_002022/-     TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
X17336/-        TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
M81579/-        TATGATAGTGATGAACCTGAATTAAGGTCACTTTCAAGCTGGATCCAGAA
AF348174/-      TATGATAGTGACGAACCTGAATTAAGGTCACTTTCAAGCTGGATCCAGAA
AF257193/-      TACCACAGTGATGAGCCAGAGCTTAGATCGCTAGCAAGCTGGATCCAGAA
AF257191/-      TATCAAAGTGATGAGCCAGAGCTCAGATCGATAGCAAGCTGGATCCAGAC


NC_002022/-     TGAGTTCAACAAGGCATGCGAACTGACAGATTCAAGCTGGATAGAGCTTG
X17336/-        TGAGTTCAACAAGGCATGTGAACTGACCGATTCAAGCTGGATAGAGCTCG
M81579/-        TGAGTTCAACAAGGCATGCGAGCTGACCGATTCAACTTGGATAGAGCTCG
AF348174/-      TGAGTTCAACAAGGCATGCGAGCTGACCGATTCAACTTGGATAGAGCTCG
AF257193/-      TGAGTTCAACAAGGCATGTGAATTGACCGATTCGAGCTGGATAGAACTTG
AF257191/-      TGAGTTCAACAAGGCATGTGAATTGACCGATTCGAGCTGGATAGAACTCG


NC_002022/-     ATGAGATTGGAGAAGATGTGGCTCCAATTGAACACATTGCAAGCATGAGA
X17336/-        ATGAGATTGGAGAAGATGCGGCTCCAATTGAACACATTGCAAGCATGAGA
M81579/-        ATGAGATTGGAGAAGATGTGGCTCCAATTGAACACATTGCAAGCATGAGA
AF348174/-      ATGAGATTGGAGAAGACGTGGCTCCAATTGAATACATTGCAAGCATGAGA
AF257193/-      ATGAGATAGGGGAAGATGTTGCCCCAATTGAGCACATTGCAAGTATGAGA
AF257191/-      ATGAGATAGGGGAAGATGTTGCCCCAATTGAGCACATTGCAAGCATGAGA


NC_002022/-     AGGAATTATTTCACATCAGAGGTGTCTCACTGCAGAGCCACAGAATACAT
X17336/-        AGGAATTATTTCACAGCAGAGGTGTCTCATTGCAGAGCCACAGAATATAT
M81579/-        AGGAATTACTTCACAGCAGAGGTGTCTCAGTGCAGAGCCACAGAATATAT
AF348174/-      AGGAATTACTTCACAGCAGAGGTGTCCCATTGCAGGGCTACTGAGTACAT
AF257193/-      AGGAACTACTTCACAGCGGAGGTGTCCCATTGCAGGGCTACTGAGTACAT
AF257191/-      AGGAACTACTTCACAGCGGAAGTGTCTCATTGCAGGGCCACTGAGTACAT


NC_002022/-     AATGAAGGGGGTGTACATCAATACTGCCTTACTTAATGCATCTTGTGCAG
X17336/-        AATGAAGGGGGTGTACATCAATACTGCCTTGCTTAATGCATCCTGTGCAG
M81579/-        AATGAAGGGGGTATACATTAATACTGCCTTGCTTAATGCATCCTGTGCAG
AF348174/-      AATGAAGGGGGTATACATTAATACTGCCTTGCTTAATGCATCCTGTGCAG
AF257193/-      AATGAAGGGGGTTTACATAAATACAGCTTTGCTCAATGCATCTTGTGCAG
AF257191/-      AATGAAGGGGGTTTACATAAATACAGCTTTGCTCAATGCATCTTGTGCAG


NC_002022/-     CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
X17336/-        CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAA
M81579/-        CAATGGACGATTTCCAACTAATTCCCATGATAAGCAAATGTAGAACTAAA
AF348174/-      CAATGGACGATTTCCAACTAATTCCCATGATAAGCAAGTGTAGAACTAAA
AF257193/-      CCATGGATGACTTCCAACTGATTCCAATGATAAGCAAATGCAGAACAAAA
AF257191/-      CCATGGATGACTTCCAACTGATTCCAATGATAAGCAAATGCAGAACAAAA


NC_002022/-     GAGGGAAGGCGAAAGACCAACTTGTATGGTTTCATCATAAAAGGAAGATC
X17336/-        GAGGGAAGGCGAAAGACCAATTTGTACGGTTTCATCATAAAAGGAAGATC
M81579/-        GAGGGAAGGCGAAAGACCAATTTATATGGTTTCATCATAAAAGGAAGATC
AF348174/-      GAAGGAAGGCGAAAGACCAATTTATATGGCTTCATCATAAAAGGAAGATC
AF257193/-      GAAGGAAGGAGGAGGACAAACCTGTATGGGTTCATTGTAAAAGGAAGGTC
AF257191/-      GAAGGAAGAAGGAAGACAAACCTGTATGGGTTCATTATAAAAGGAAGGTC


NC_002022/-     CCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
X17336/-        CCACTTAAGGAATGACACCGATGTGGTAAACTTTGTGAGCATGGAGTTTT
M81579/-        TCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
AF348174/-      TCACTTAAGGAATGACACCGACGTGGTGAACTTTGTGAGTATGGAATTGT
AF257193/-      CCATTTGAGAAATGATACTGACGTGGTGAACTTTGTGAGTATGGAATTCT
AF257191/-      CCATTTGAGAAATGATACTGACGTGGTGAACTTTGTGAGTATGGAATTCT
```

Figure 9

```
NC_002022/-    CTCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
X17336/-       CGCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
M81579/-       CTCTCACTGACCCAAGACTTGAGCCACACAAATGGGAGAAGTACTGTGTT
AF348174/-     CTCTCACTGACCCGAGACTTGAGCCACACAAATGGGAGAATTACTGTGTC
AF257193/-     CGCTTACTGACCCAAGGCTGGAGCCACACAAATGGGAAAAGTACTGTGTT
AF257191/-     CGCTTACTGACCCAAGGCTGGAGCCACACAAATGGGAAAAGTACTGTGTT


NC_002022/-    CTTGAGATAGGAGATATGCTTCTAAGAAGTGCCATAGGCCAGGTTTCAAG
X17336/-       CTTGAGGTAGGAGATATGCTTCTAAGAAGTGCCATAGGCCATGTGTCAAG
M81579/-       CTTGAGATAGGAGATATGCTACTAAGAAGTGCCATAGGCCAGGTGTCAAG
AF348174/-     CTTGAGATAGGAGATATGCTACTAAGAAGTGCTATAGGCCAGATGTCAAG
AF257193/-     CTTGAAATAGGGGAAATGCTCTTGCGGACTGCAATAGGTCAAGTGTCAAG
AF257191/-     CTTGAAGTAGGGGAAATGCTCTTGCGGACTGCAATAGGCCAGGTGTCAAG


NC_002022/-    GCCCATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAAATTAAAATGA
X17336/-       GCCTATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAAATTAAAATGA
M81579/-       GCCCATGTTCTTGTATGTGAGGACAAATGGAACATCAAAGATTAAAATGA
AF348174/-     GCCTATGTTCTTGTATGTGAGAACAAATGGAACATCAAAGATTAAAATGA
AF257193/-     GCCCATGTTCCTGTATGTGAGAACCAACGGAACCTCAAAAAATTAAGATGA
AF257191/-     GCCCATGTTCCTGTATGTGAGAACTAACGGAACCTCCAAAATTAAGATGA


NC_002022/-    AATGGGGAATGGAGATGAGGCGTTGTCTCCTCCAGTCACTTCAACAAATT
X17336/-       AATGGGGGATGGAAATGAGGCGTTGCCTCCTTCAGTCACTTCAACAAATC
M81579/-       AATGGGGAATGGAGATGAGGCGTTGCCTCCTTCAGTCACTCCAACAAATC
AF348174/-     AATGGGGAATGGAGATGAGGCGTTGCCTCCTTCAGTCACTCCAACAAATC
AF257193/-     AATGGGGGATGGAAATGAGGCGCTGCCTTCTTCAATCTCTTCAACAGATT
AF257191/-     AATGGGGGATGGAAATGAGACGCTGCCTTCTTCAATCTCTTCAACAGATT


NC_002022/-    GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAAGAGAAAGACATGACCAA
X17336/-       GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAGGAGAAAGACATGACCAA
M81579/-       GAGAGTATGATTGAAGCCGAGTCCTCTGTCAAGGAGAAAGACATGACCAA
AF348174/-     GAGAGTATGATTGAAGCAGAGTCATCTGTCAAAGAGAAAGACATGACCAA
AF257193/-     GAGAGCATGATCGAGGCTGAGTCTTCTATCAAAGAGAAAGACATGACCAA
AF257191/-     GAGAGCATGATCGAGGCTGAGTCTTCTATCAAAGAGAAAGACATGACCAA


NC_002022/-    AGAGTTCTTTGAGAACAAATCAGAAACATGGCCCATTGGAGAGTCTCCCA
X17336/-       AGAGTTCTTTGAAAACAAATCAGAAACATGGCCCGTTGGAGAGTCCCCCA
M81579/-       AGAGTTTTTCGAGAATAAATCAGAAACATGGCCCATTGGAGAGTCCCCCA
AF348174/-     AGAGTTTTTTGAGAATAAATCAGAAACATGGCCCATTGGGGAGTCCCCCA
AF257193/-     AGAATTCTTTGAAAACAGATCGGAGACATGGCCAATTGGAGAGTCACCTA
AF257191/-     AGAATTCTTTGAAAACAGATCGGAGACATGGCCAATTGGAGAGTCACCTA


NC_002022/-    AAGGAGTGGAGGAAAGTTCCATTGGGAAGGTCTGCAGGACTTTATTAGCA
X17336/-       AAGGAGTGGAGGAAGGTTCCATTGGGAAGGTCTGCAGAACTTTATTGGCA
M81579/-       AAGGAGTGGAAGAAGGTTCCATTGGGAAGGTCTGCAGGACTTTATTGGCC
AF348174/-     AGGGAGTGGAAGATGGTTCCCATGGGGAAGGTGTGCAGAACCTTACTAGCA
AF257193/-     AGGGAGTGGAGGAAGGCTCCATCGGGAAGGTGTGCAGAACCTTACTAGCA
AF257191/-     AGGGAGTGGAGGAAGGCTCAATCGGGAAGGTGTGCAGAACCTTACTAGCA


NC_002022/-    AAGTCGGTATTTAACAGCTTGTATGCATCTCCACAACTAGAAGGATTTTC
X17336/-       AAGTCGGTATTCAACAGCTTGTATGCATCTCCACAACTGGAAGGATTTTC
M81579/-       AAGTCGGTATTCAATAGCCTGTATGCATCTCCACAATTAGAAGGATTTTC
AF348174/-     AAGTCGGTATTCAATAGCCTGTATGCATCCCCGCAATTGGAAGGGTTTTC
AF257193/-     AAATCTGTGTTCAACAGCCTATATTCATCTCCACAACTCGAAGGATTTTC
AF257191/-     AAATCTGTGTTCAACAGCCTATATTCATCTCCACAACTCGAAGGATTTTC


NC_002022/-    AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAATC
X17336/-       AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAAGC
```

Figure 9

```
M81579/-     AGCTGAATCAAGAAAACTGCTTCTTGTCGTTCAGGCTCTTAGGGACAATC
AF348174/-   AGCTGAGTCAAGAAAACTGCTTCTTGTCGTTCAGGCTCTTAAGGACAATC
AF257193/-   AGCTGAATCGAGAAAACTACTACTCATTGTTCAAGCACTTAGGGACAACC
AF257191/-   AGCTGAATCGAGAAAACTACTACTCATTGTTCAAGCACTTAGGGACAACC


NC_002022/-  TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
X17336/-     TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
M81579/-     TTGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
AF348174/-   TTGAACCTGGAACCTTTGATCTTGAGGGGCTATATGAAGCAATTGAGGAG
AF257193/-   TGGAACCTGGAACCTTCGATCTTGAAGGGCTATATGGAGCAATTGAGGAG
AF257191/-   TGGAACCTGGAACCTTTGATCTTGAAGGGCTATATGGAGCAATTGAGGAG


NC_002022/-  TGCCTAATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
X17336/-     TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCGTCTTGGTTCAACTC
M81579/-     TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCGTCGTGGTTCAACTC
AF348174/-   TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF257193/-   TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF257191/-   TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC


NC_002022/-  CTTCCTTACACATGCATTGAGTTAGTTGTGGCAGTGCTACTATTTGCTAT
X17336/-     CTTCCTCACACATGCATTGAGATAGTTGTGGCAATGCTACTATTTGCTAT
M81579/-     CTTCCTAACACATGCATTAAGATAGTTGTGGCAATGCTACTATTTGCTAT
AF348174/-   CTTCCTAACACATGCATTAAGATAGTTGTGGCAATGCTACTATTTGCTAT
AF257193/-   CTTCCTCACACATGCACTAAGATAGTTGTGGCAATGCTACTATTTGCTAT
AF257191/-   CTTCCTCACACATGCACTAAAATAGTTGTGGCAATGCTACTATTTGCTAT


NC_002022/-  CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--     (SEQ ID NO: 121)
X17336/-     CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--     (SEQ ID NO: 122)
M81579/-     CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--     (SEQ ID NO: 123)
AF348174/-   CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--     (SEQ ID NO: 124)
AF257193/-   CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--     (SEQ ID NO: 125)
AF257191/-   CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--     (SEQ ID NO: 126)
```

Figure 10

CLUSTAL W(1.4) multiple sequence alignment

Shaded area: selected siRNA sequence.

NC_002022	A/Puerto Rico/8/34	H1N1	1934	2233 nt
X17336	A/WSN/33	H1N1	1933	2233 nt
M21850	A/chicken/FPV/Rostock/34	H7N1	1934	2233 nt
AF156457	A/turkey/California/189/66	H9M2	1966	2140 nt
M26087	A/Equine/London/1416/73	H7N7	1973	2233 nt
M26088	A/gull/Maryland/704/77	H13N6	1977	2233 nt
AF222820	A/swine/Hong Kong/9/98	H9N2	1998	1635 nt

```
NC_002022/-   AGCGAAAGCAGGTACTGATCCAAAATGGAAGATTTTGTGCGACAATGCTT
X17336/-      AGCGAAAGCAGGTACTGATTCAAAATGGAAGATTTTGTGCGACAATGCTT
M21850/-      AGCGAAAGCAGGTACTGATCCAAAATGGAAGACTTCGTGCGACAATGCTT
AF156457/-    -------------------ATGGAAGACTTCGTGCGACAATGCTT
M26087/-      AGCAAAAGCAGGTACTGATCCAAAATGGAAGACTTTGTGCGACAATGCTT
M26088/-      AGCAAAAGCAGGTACTGATTCAAAATGGAAGACTTTGTGCGACAATGCTT
AF222820/-    --------------------------------------------------


NC_002022/-   CAATCCGATGATTGTCGAGCTTGCGGAAAAAACAATGAAAGAGTATGGGG
X17336/-      CAATCCGATGATTGTCGAGCTTGCGGAAAAGGCAATGAAAGAGTATGGAG
M21850/-      CAATCCAATGATCGTCGAGCTTGCGGAAAAGACAATGAAAGAATATGGAG
AF156457/-    CAATCCAATGATTGTCGAGCTTGCGGAAAAGGCAATGAAAGAATATGGAG
M26087/-      CAATCCAATGATCGTCGAGCTTGCGGAAAAGGCGATGAAAGAATATGGAG
M26088/-      CAATCCAATGATCGTCGAGCTTGCGGAAAAGGCAATGAAAGAATATGGAG
AF222820/-    --------------------------------------------------


NC_002022/-   AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCACTTG
X17336/-      AGGACCTGAAAATCGAAACAAACAAATTTGCAGCAATATGCACACATTTG
M21850/-      AGGACCCGAAGATTGAAACAAACAAATTCGCAGCAATATGCACTCATTTG
AF156457/-    AGGGCCCGAAAATCGAAACAAACAAATTTGCAGCAATATGCACTCATTTG
M26087/-      AGGACCCGAAAATTGAAACAAACAAATTTGCAGCAATATGCACCACCTTG
M26088/-      AGGATCCAAAAATCGAGACAAACAAATTCGCTGCAATATGCACACACCTG
AF222820/-    --------------------------------------------------


NC_002022/-   GAAGTATGCTTCATGTATTCAGATTTCCACTTCATCAATGAGCAAGGCGA
X17336/-      GAAGTGTGCTTCATGTATTCAGATTTCCACTTCATCGATGAGCAAGGCGA
M21850/-      GAAGTGTGTTTCATGTATTCAGATTTCCACTTTATTGATGAACGGGGAGA
AF156457/-    GAAGTGTGTTTCATGTATTCAGACTTCCACTTCATCGATGAGCGAGGCGA
M26087/-      GAAGTCTGCTTCATGTACTCGGATTTCCACTTTATTAATGAACTGGGCGA
M26088/-      GAAGTGTGTTTCATGTATTCAGACTTCCATTTCATTGATGAACGGGGTGA
AF222820/-    --------------------------------------------------


NC_002022/-   GTCAATAATCGTAGAACTTGGTGATCCTAATGCACTTTTGAAGCACAGAT
X17336/-      GTCAATAGTCGTAGAACTTGGGGATCCAAATGCACTTTTGAAGCACCGAT
M21850/-      GTCAAAGATTGTAGAATCTGGTGACCCAAATGCACTCTTGAAGCACAGAT
AF156457/-    ATCAATAATTGTAGAATCCGGGAGATCCGAATGCCCTCTTGAAGCACAGAT
M26087/-      GTCAGTGATCATAGAGTCTGGTGATCCAAATGCTCTTTTGAAACATCGAT
M26088/-      GTCGATAATTGTTGAGTCTGGTGATCCAAATGCACTCTTAAAACATCGAT
AF222820/-    --------------------------------------------------


NC_002022/-   TTGAAATAATCGAGGGAAGAGATCGCACAATGGCCTGGACAGTAGTAAAC
X17336/-      TTGAAATAATCGAGGGAAGAGATCGCACAATAGCCTGGACAGTAATAAAC
M21850/-      TTGAGATAATTGAAGGAAGAGATCGCACGATGGCCTGGACGGTGGTGAAT
AF156457/-    TTGAAATAATTGAGGGAAGAGATCGCACAATGGCCTGGACAGTGGTGAAC
M26087/-      TTGAAATGATTGAAGGGAGAGATCGAACAATGGCATGGACAGTAGTGAAC
M26088/-      TTGAAATAATCGAAGGAAGAGACCGTACTATGGCCTGGACAGTGGTGAAT
AF222820/-    --------------------------------------------------
```

Figure 10

<pre>
NC_002022/-   AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
X17336/-   AGTATTTGCAACACTACAGGGGCTGAGAAACCAAAGTTTCTACCAGATTT
M21850/-   AGCATTTGCAATACTACAGGGGTTGAGAAACCAAGTTCCTTCCGGATTT
AF156457/-   AGCATCTGTAACACTACAGGGGTTGAGAAGCCAAGGTTTCTCCCAGATCT
M26087/-   AGTATCTGCAACACCACAAGAGCTGAAAAACCAAGTTCCTCCCAGATTT
M26088/-   AGCATTTGCAACACCACAGGAGTTGAGAAGCCAAAGTTTCTTCCGGACTT
AF222820/-   --

NC_002022/-   GTATGATTACAAGGAAAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
X17336/-   GTATGATTACAAGAAGAATAGATTCATCGAAATTGGAGTAACAAGGAGAG
M21850/-   GTATGATTATAAGGAGAACCGGATTCATTGAGATTGGAGTGACAAGGAGAG
AF156457/-   ATATGACTACAAGGAGAACAGGTTCATTGTTGAAATTGGTGTGACAAGGAGAG
M26087/-   GTAGGACTATAAAGAGAACAGGTTTGTTGAAATTGGAGTGACAAGGAGAG
M26088/-   ATATGATTATAAAGAAAATCGTTTCATTGAAATTGGAGTGACAAGGAGGG
AF222820/-   --

NC_002022/-   AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAA
X17336/-   AAGTTCACATATACTATCTGGAAAAGGCCAATAAAATTAAATCTGAGAAG
M21850/-   AGGTCCACATATACTACTTAGAAAAAGCCAATAAGATAAAATCTGAGAAG
AF156457/-   AAGTCCACATATACTACCTGGAAAAGGCCAATAAAATAAAGTCTGAGAAG
M26087/-   AAGTTCACATATACTACTTGGAGAAGGCCAACAAAATAAAGTCTGAGAAA
M26088/-   AGGTCCATATATACTATCTAGAAAAGGCCAATAAGATAAAGTCTGAGAAG
AF222820/-   --

X17336/-   ACACACATCCACATTTTCTCATTCACTGGGGAGGAAATGGCCACAAAGGC
M21850/-   ACACACATCCACATCTTCTCATTCACTGGGGAAGAAATGGCCACTAAGGC
NC_002022/-   ACACACATCCACATTTTCTCGTTCACTGGGGAAGAAATGGCCACAAAGGC
AF156457/-   ACACATATCCACATCTTCTCGTTCACAGGAGAAGAGATGGCCACAAAGGC
M26087/-   ACACATATTCACATTTTCTCATTACAGGAGAGGAAATGGCCACAAAAGC
M26088/-   ACACACATCCATATCTTTTCATTCACTGGAGAAGAAATGGCCACAAAAGC
AF222820/-   --

NC_002022/-   CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
X17336/-   CGACTACACTCTCGATGAAGAAAGCAGGGCTAGGATCAAAACCAGGCTAT
M21850/-   GGACTACACTCTTGATGAAGACAGCAGAGCAAGGATCAAAACCAGGCTAT
AF156457/-   TGACTACACTCTTGATGAAGAAAGTAGGGCCAGAATCAAAACTAGACTGT
M26087/-   GGATTATACGCTTGATGAAGAAAGTAGAGCCAGGATCAAAACCAGACTAT
M26088/-   AGACTACACTCTTGATGAAGAGAGTAGAGCAAGGATCAAAACCAGACTAT
AF222820/-   ---------------AGCAAAAGCAGGGCAAGGATCAAAACTAGGCTGT

NC_002022/-   TCACCATAAGACAAGAAATGGCCAGCAGAGGCCTCTGGGATTCCTTTCGT
X17336/-   TCACCATAAGACAAGAAATGGCTAGCAGAGGCCTCTGGGATTCCTTTCGT
M21850/-   TCACCATAAGACAAGAAATGGCCAGTAGAGGCCTCTGGGATTCCTTTCGT
AF156457/-   TCACCATAAGGCAGGAAATGGCCAGTAGAGGTCTCTGGGATTCCTTTCGT
M26087/-   TCACCATAAGACAAGAAATGGCCAGCAGAGGCCTTTGGGAGTCCTTTCGT
M26088/-   TCACTATAAGACAAGAAATGGCCAGTAGAGGTCTCTGGGATTCCTTTCGT
AF222820/-   TCACCATAAGACAGGAAGTGGCTAGCAGGGGTCTATGGGATTCCTTTCGT

NC_002022/-   CAGTCCGAGAGAGGAGAAGAGACAATTGAAGAAAGGTTTGAAATCACAGG
X17336/-   CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M21850/-   CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
AF156457/-   CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG
M26087/-   CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATTACAGG
M26088/-   CAGTCCGAGAGAGGCGAAGAGACAATTGAAGAAAGATTTGAAATCACAGG

NC_002022/-   AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCGAACTTCTCCAGCC
X17336/-   AACAATGCGCAAGCTTGCCGACCAAAGTCTCCCGCCAAACTTCTCCAGCC
M21850/-   AACCATGCGCAGGCTTGCCGAACAAAGTCTCCCACCGAACTTCTCCAGCC
AF156457/-   AACAATGCGCAGGCTTGCCGACCAAAGTCTCCCACCGAACTTCTCCAGCC
</pre>

Figure 10

```
M26087/-      GACAATGCGCAGGCTTGCCGATTACAGTCTCCCACCGAACTTCTCCAGCC
M26088/-      AACGATGCGCAGGCTCGCCGACCAAAGTCTCCCACCGAACTTCTCCAGCC
AF222820/-    AACAATGCGCAGGCTTGCCGACCAAAGTCTCCCACCGAATTTCTCCAGCC


NC_002022/-   TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
X17336/-      TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTACATT
M21850/-      TTGAAAACTTTAGAGCCTATGTGGATGGATTCAAACCGAACGGCTGCATT
AF156457/-    TTGAAAACTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT
M26087/-      TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT
M26088/-      TTGAAAACTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT
AF222820/-    TTGAAAATTTTAGAGCCTATGTGGATGGATTCGAACCGAACGGCTGCATT


NC_002022/-   GAGGGCAAGCTGTCTCAAATGTCCAAAGAAGTAAATGCTAGAATTGAACC
X17336/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCAAGAATGGAGCC
M21850/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTGAATGCAAGAATTGAACC
AF156457/-    GAGAGCAAGCTTTCTCAAATGTCAAAAGAAGTAAATACCAGAATGGAGCC
M26087/-      GAGGGCAAGCTTTCTCAAATGTCCAAAGAAGTAAATGCAAGAATTGAACC
M26088/-      GAGGGCAAGCTTTCTCAGATGTCAAAAGAAGTAACCGCCAGAATTGAGCC


NC_002022/-   TTTTTTGAAAACAACACCACGACCACTTAGACTTCCGAATGGGCCTCCCT
X17336/-      TTTTTTGAAATCAACACCACGACCACTTAGACTTCCGGATGGGCCTCCCT
M21850/-      ATTGTTGAAGACAACACCACGCCCTCTCAGATTACCTGATGGGCCTCCCT
AF156457/-    CTTTTTGAAGACAACACCACGCCCACTCAAGCTACCAGATGGGCCTCCCT
M26087/-      ATTTTCAAAGACAACACCGCGGCCACTCAGGAGACCGGGTGGTCCACCCT
M26088/-      ATTTTTGAAGACAACACCACGCCCTCTCAGATTACCAGAGGGGCCTCCCT
AF222820/-    CTTTGTTAAAACAACACCACGTCCTCTAAGACTGCCGGGGTGGACCTCCCT


NC_002022/-   GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCCTTAAAATTAAGCATT
X17336/-      GTTCTCAGCGGTCCAAATTCCTGCTGATGGATGCTGTGAAATTAAGCATT
M21850/-      GTTCTCAGCGGTCAAAATTCCTACTGCTAATGGACGCTTTGAAATTAAGCATT
AF156457/-    GCTCCCAGCGGTCCAAATTCCTGCTGATGGATGCTCTGAAATTTAGCATT
M26087/-      GTTATCAGCGATCCAAATTCTTGCTGATGGATGCTCTGAAATTTAGCATT
M26088/-      GCTCTCAGCGGTCAAAATTCTGTTGATGGATGCTCTGAAGCTTAGCATT
AF222820/-    GTTCCCAAAGGTCAAAATTCTTACTGATGGATGCTCTGAAATTAAGCATT


NC_002022/-   GAGGACCCAAGTCATGAAGGAGAGGGAATACCGCTATATGATGCAATCAA
X17336/-      GAGGACCCAAGTCATGAGGGAGAGGGGATACCGCTATATGATGCAATCAA
M21850/-      GAGGACCCAAGTCATGAGGGCGAGGGGATACCACTACATGATGCAATCAA
AF156457/-    GAGGACCCAAGCCATGAAGGAGAAGGGATACCGCTATATGATGCAATCAA
M26087/-      GAGGATCCAAGTCACGAGGGAGAGGGAATACCGCTGTATGATGCCATCAA
M26088/-      GAAGACCCGAGTCATGAGGGTGAGGGAATACCACTGTATGATGCTATCAA
AF222820/-    GAGGACCCGAGTCATGAGGGAGAGGGGATACCGCTGTATGATGCGATCAA


NC_002022/-   ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
X17336/-      ATGCATGAGAACATTCTTTGGATGGAAGGAACCCAATGTTGTTAAACCAC
M21850/-      ATGCATGAGGACATTCTTTGGCTGGAAAGAGCCCAATATTGTCAAACCGC
AF156457/-    ATGCATGAAAACATTCTTTGGGTGGAAAGAGACCCAATATTGTTAAACCAC
M26087/-      ATGCATGAAAACCTTCTTTGGCTGGAAAGAGCCCAACATTGTCAAGCCAC
M26088/-      ATGTATGAAGACCTTTTTTGGCTGGAAAGAGCCCAAAATTATCAAGTCAC
AF222820/-    ATGCATGAAAACATTTTTCGGCTGGAAAGAGCCCAAAATTATCAAGTCAC


NC_002022/-   ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
X17336/-      ACGAAAAGGGAATAAATCCAAATTATCTTCTGTCATGGAAGCAAGTACTG
M21850/-      ATGAGAAGGGCATAAATCCCAAGTATCTCCTGGCTTGGAACCAGGTGCTA
AF156457/-    ATGAAAAGGGAATAAATCCGAATTAGCTCTTGGCATGGAAACAAGTACTA
M26087/-      ATGAAAAGGGTATAAACCCAAAGTATCTCCAGGCTTGGAAGCAAGTGTTA
M26088/-      ATGAGAGGGGCATAAACCCTAATTATCTCCTGGCTTGGAAGCAAGTGCAA
AF222820/-    ATGAGAAGGGTATAAACCCAAATTATCTCCTAGCTTGGAAGCAGGTGCTG
```

Figure 10

```
NC_002022/-    GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAAGACTAAAAA
X17336/-       GCAGAACTGCAGGACATTGAGAATGAGGAGAAAATTCCAAGGACTAAAAA
M21850/-       GCAGAACTGAAGGATATTGAGAATGAGGAGAAAATTCCAAAAACAAAAAA
AF156457/-     GCGGAACTACAGGATCTTGAAAATGAAGAGAAAATTCCAAAGACTAAAAA
M26087/-       GCAGAACTACAGGACGTGGAAAACGAAGAAAAATCCCTAAGACCAAGAA
M26088/-       GCAGAACTGCAGGATATTGAAAATGAAGACAAGATTCCAAAGACAAAAAA
AF222820/-     GCAGAGCTCCAGGACATTGAAAATGATGAAAAGATGCCAAAAACAAAGAA


NC_002022/-    TATGAAAAAAACAAGTCAGCTAAAGTGGGCACTTGGTGAGAACATGGCAC
X17336/-       TATGAAGAAAACGAGTCAGTTAAAGTGGGCACTTGGTGAGAACATGGCAC
M21850/-       TATGAAGAAAACAAGCCAGTTAAAGTGGGCACTTGGTGAGAATATGGCAC
AF156457/-     CATGAAGAAAACAAGCCAATTAAAGTGGGCACTTGGTGAGAATATGGCGC
M26087/-       TATGAAAAAAACAAGTCAATTGAAATGGGCACTTGGTGAGAACATGGCAC
M26088/-       CATGAAGAAAACAAGCCAATTAAAGTGGGCACTTGGTGAGAACATGGCAC
AF222820/-     CATGAAGAAAACAAGCCAATTAAAGTGGGCATTAGGTGAGAACATGGCAC


NC_002022/-    TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
X17336/-       CAGAAAAGGTAGACTTTGAGGATTGTAAAGATGTAGGCGATTTGAAGCAA
M21850/-       CAGAGAAAGTAGACTTTGAGGATTGCAAGGACATTAGCGATCTGAAGCAG
NC_002022/-    TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
AF156457/-     CAGAAAAAGTGGATTTTGAGGACTGCAAGGATGTCAGCGATCTGAAGCAA
M26087/-       CAGAGAAAGTGGATTTTGAGGATTGTAAAGACATCAGTGATTTGAAAACAG
M26088/-       CAGAGAAAGTGGACTTTGAAGATTGCAAGGATGTCAGCGATTTGAAAACAG
AF222820/-     CAGAGAAAGTGGACTTTGAGGATTGCAAAGACGTTAGTGACCTGAAACAA


NC_002022/-    TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
X17336/-       TATGATAGTGATGAACCAGAATTGAGGTCGCTTGCAAGTTGGATTCAGAA
M21850/-       TATGACAGTGATGACCCAGAACAGAGATCACTAGCGAGTTGGATCCAGAG
AF156457/-     TATGACAGTGATGAACCGGAACCGAGATCGCCTTGCAAGTTGGATTCAGAG
M26087/-       TATGACAGTGATGAGCCAGAAACAAGGTCCCTTGCAAGTTGGATTCAAAG
M26088/-       TATGACAGCGATGAGCCAGAACAAAGGTCGCTAGCAAGTTGGGTCCAAAG
AF222820/-     TATGATAGTGATGAACCAGAGCCCAAATCGCTAGCAAGTTGGATCCAGAG


NC_002022/-    TGAGTTCAACAAGGCATGCGAACTGACAGATTCAAGCTGGATAGAGCTTG
X17336/-       TGAGTTCAACAAGGCATGTGAACTGACCGATTCAAGCTGGATAGAGCTCG
M21850/-       TGAATTCAACAAAGCATGTGAGCTGACCGATTCAGGTTGGATAGAACTTG
AF156457/-     TGAGTTCAATAAGGCGTGTGAACTGACTGATTCAAGCTGGATAGAGCTTG
M26087/-       TGAGTTCAACAAAGCTTGTGAGCTGACAGATTCAAGCTGGATAGAGCTCG
M26088/-       TGAATTCAACAAAGCTTGTGAATTGACTGATTCAAGCTGGATAGAACTCG
AF222820/-     TGAATTTAACAAGGCATGTGAGTTGACCGATTCAAGCTGGGTAGAACTTG


NC_002022/-    ATGAGATTGGAGAAGATGTGGCTCCAATTGAACACATTGCAAGCATGAGA
X17336/-       ATGAGATTGGAGAAGATGCGGCTCCAATTGAACACATTGCAAGCATGAGA
M21850/-       ATGAAATAGGAGAAGATGTAGCCCCAATCGAGCACATTGCAAGTATGAGG
AF156457/-     ACGAGATTGGGGAAGATGTTGCCCCAATTGAGCACATTGCAAGCATGAGG
M26087/-       ATGAAATTGGGGAGGATGTTGCCCCAATAGAACACATTGCCAGCATGAGG
M26088/-       ATGAAATAGGGGAAAATGTCGCCCCAATCGAGCATATTGCAAGCATGAGG
AF222820/-     ATGAAATAGGAGAAGATGTTGCTCCAATCGAGCACATTGCGAGTATGAGA


NC_002022/-    AGGAATTATTTCACATCAGAGGTGTCTCACTGCAGAGCCACAGAATACAT
X17336/-       AGGAATTATTTCACAGCAGAGGTGTCTCATTGCAGAGCCACAGAATACAT
M21850/-       AGAAAGTATTTCACAGCGGAAGTGTCTCACTGCAGGGCAAACGGAGTACAT
AF156457/-     AGGAATTATTTCACAGCGGAGGTGTCTCATTGTAGAGCCACAGAATACAT
M26087/-       AGGAATTATTTTACTGCTGAGGTTTCCCATTGTAGAGCAACTGAATATAT
M26088/-       AGGAATTATTTTACAGCTGAAGTGTCTCACTGCAGGGCAACAGAGTACAT
AF222820/-     AGGAATTAGTTCACAGCAGAAGTGTCACACTGCGGGGCTACTGAGTATAT


NC_002022/-    AATGAAGGGGGTGTACATCAATACTGCCTTACTTAATGCATCTTGTGCAG
X17336/-       AATGAAGGGGGTGTACATCAATACTGCCTTGCTTAATGCATCGTGTGCAG
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4 of 7

Figure 10

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M21850/-      AATGAAAGGGGTATACATAAACACGGCCTTGCTCAATGCATCTTGTGCAG
AF156457/-    AATGAAAGGGGTATACATCAATACTGCCTTGCTCAATGCATCGTGTGCGG
M26087/-      AATGAAGGGAGTATACATCAACACTGCTCTACTCAATGCATCCTGCGCTG
M26088/-      AATGAAGGGAGTGTACATAAACTCAGCTTTACTCAAGGCCTCTTGTGCAG
AF222820/-    AATGAAGGGAGTGTATATTAACACAGCGTTGCTCAATGCATCTTGTGCAG


NC_002022/-   CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
X17336/-      CAATGGATGATTTCCAATTAATTCCAATGATAAGCAAGTGTAGAACTAAG
M21850/-      CTATGGATGACTTCCAGGCTGATGCCAATGATAAGCAAATGCAGGGACCAAA
AF156457/-    CTATGGATGACTTTCAACTGATTCCAATGATCAGCAAGTGTAGAACTAAA
M26087/-      CGATGGATGACTTCCAATTAATGCCCATGATAAGCAAATGCAGGGACCAAG
M26088/-      CCATGGATGATTTTCAGTTGATCCCAATGATAAGCAAATGCAGAACCAAA
AF222820/-    CCATGGATGACTTCCAATTGATTCCAATGATAAGCAAATGCAGAACAAAA


NC_002022/-   GAGGGAAGGCGAAAGACCAACTTGTATGGTTTCATCATAAAAGGAAGATC
X17336/-      GAGGGAAGGCGAAAGACCAATTTGTACGGTTTCATCATAAAAGGAAGATC
M21850/-      GAAGGAAGACGCGAAGACGAATCTGTATGGATTCATTATAAAAGGAAGATC
AF156457/-    GAGGGAAGAAGAAAGACAAATTTGTATGGGTTCATTATAAAAGGGAGATC
M26087/-      GAAGGGAGAAGCGAAGACAAATTTGTATGGATTCATCATAAAGGGAAGGTC
M26088/-      GAAGGACGACGGAAAACAAATTTGTATGGATTCATCATAAAGGGAAGGTC
AF222820/-    GAAGGGAGACGGAAAACAAACCTGTATGGGTTCATTATCAAGGGAAGGTC


NC_002022/-   CCACTTAAGGAATGACACCGACGTGGTAAACTTTGTGAGCATGGAGTTTT
X17336/-      CCACTTAAGGAATGACACCGATGTGGTAAACTTTGTGAGCATGGAGTTTT
M21850/-      TCACTTGAGGAATGATACTGATGTGGTGAATTTTGTGAGCATGGAGTTGT
AF156457/-    CCACCTGAGGAACGACACCGATGTGGTAAACTTTGTGAGCATGGAGTTTT
M26087/-      CCATTTAAGAAATGACACTGACGTGGTGGAATTTGTGAGCATGGAGTTTT
M26088/-      TCATTTGAGGAATGATACTGATGTGGTGAATTTTGTGAGCATGGAATTTT
AF222820/-    CCATTTGAGGAATGATACTGATGTGGTAAACTTTGTGAGCATGGAATTTT


NC_002022/-   CTCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
X17336/-      CCCTCACTGACCCAAGACTTGAACCACACAAATGGGAGAAGTACTGTGTT
M21850/-      CTCTCACTGACCCGAGGCTTGAGCCACACAAGTGGGAGAAGTATTGTGTT
AF156457/-    CCCTCACTGACCCGAGGCTTGAACCGCACAAATGGGAGAAGTACTGTGTT
M26087/-      CTCTCACCGATCCAAGACTTGAGCCACACAATTGGGAGAAGTACTGTGTT
M26088/-      CTCTTACTGACCCTAGATTAGAACCACACAAGTGGGAGAAGTATTGTGTC
AF222820/-    CTCTTACAGACCCGAAACTGGAACCACACAAGTGGGAGAAGTACTGTGTT


NC_002022/-   CTTGAGATAGGAGATATGCTTCTAAGAAGTGCCATAGGCCAGGTTTCAAG
X17336/-      CTTGAGGTAGGAGATATGCTTCTAAGAAGTGCCATAGGCCATGTGTCAAG
M21850/-      CTTGAAATAGGAGACATGCTCCTGCGGACTGCAATAGGCCAAGTTTCGAG
AF156457/-    CTTGAAATAGGGGACATGCTTCTCTAAGAACTGCTGTAGGCCAAGTGTCAAG
M26087/-      CTAGAAATCGGAGACATGCTCCTACGAACTGCAATAGGCCAAGTTTCAAG
M26088/-      CTTGAAATAGGGGATATGCTCCTGCGGAACTTCAATAGGCCAGGTGTCAAG
AF222820/-    CTTGAAGTAGGGGACATGCTCCTGCGAGAACTTCAATAGGCCAGGTGTCAAG


NC_002022/-   GCCCATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAAATTAAAATGA
X17336/-      GCCTATGTTCTTGTATGTGAGGACAAATGGAACCTCAAAAAATTAAAATGA
M21850/-      GCCCATGTTCCTGTATGTGAGAACCAATGGAACCTCCAAAATCAAGATGA
AF156457/-    GCCCATGTTCCTGTATGTGAGAACGAATGGGACCTCCAAAATCAAAATGA
M26087/-      ACCCATGTTTTTGTATGTAAGGACCAATGGGACCTCTAAAATTAAAATGA
M26088/-      ACCCATGTTCTGTATGTGACAACCAATGGAACTTCCAAGATGAAAATGA
AF222820/-    GCCCATGTTCCTATAGGTGAGAACCAATGGAACCTCCAAAATTAAAATGA


NC_002022/-   AATGGGGAATGGAGATGAGGCGTTGTCTCCTCCAGTCACTTCAACAAATT
X17336/-      AATGGGGCATGGAAATGAGGCGTTGCCTCCTTCAGTCACTTCAACAAATC
M21850/-      AATGGGGTATGGAAATGAGACGCTGTCTTCTCCAGTCCCTTCAACAGGTT
AF156457/-    AATGGGGCATGGAAATGAGACGCTGTCTTCTCCAGTCCCTTCAACAAATT
M26087/-      AATGGGGAATGGAAATGAGGCGCTGCCTCCTTCAGTCTCTACAGCACATT
M26088/-      AATGGGGTATGGAGATGAGGCGTTGTCTTCTTCAATCCCTCCAGCAAATC
```

Figure 10

```
AF222820/-      AATGGGGAATGGAGATGAGGCGTTGCCTCCTTCAATCCCTTCAACAAATT


NC_002022/-     GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAAGAGAAAGACATGACCAA
X17336/-        GAGAGTATGATTGAAGCTGAGTCCTCTGTCAAGGAGAAAGACATGACCAA
M21850/-        GAAAGCATGGTTGAGGCTGAGTCCTCTGTCAAGGAGAAAGACATGACTAA
AF156457/-      GAGAGTATGATTGAAGCGGAGTCCTCTGTCAAAGAGAAGGACATGACCAA
M26087/-        GAAAGCATGACTGAAGCTGAGTCCTCAGTCAAAGAAAAGGACATGACCAA
M26088/-        GAAAGCATGATTGAGGCCGAGTCCTCTGTCAAGGAAAAAGACATGACTAA
AF222820/-      GAGAGCATGATTGAGGCAGAGTCTTCTATCAAAGAGAAGGACATGACCAA


NC_002022/-     AGAGTTCTTTGAGAACAAATCAGAAACATGGCCCATTGGAGAGTCTCCCA
X17336/-        AGAGTTCTTTGAAAACAAATCAGAAACATGGCCCGTTGGAGAGTCCCCCA
M21850/-        GGAATTCTTTGAAAACAAGTCAAAGACGTGGCCCATTGGAGAATCACCTA
AF156457/-      AGAGTTCTTTGAAAACAAATCAGAAACATGGCCTATTGGGGAATCTCCCA
M26087/-        AGAATTCTTTGAGAACAAATCGGAGACATGGCCTATAGGAGAGTCCCCCA
M26088/-        AGAATTCTTTGAAAACAAGTCGGAGACATGGCCCATTGGAGAATCACCCA
AF222820/-      AGAATTCTTTGAAAACAAGTCGGAGACGTGGCCGATTGGAGAGTCACCTA


NC_002022/-     AAGGAGTGGAGGAAAGTTCCATTGGGAAGGTCTGCAGGACTTTATTAGCA
X17336/-        AAGGAGTGGAGGAAGGTTCCATTGGGAAGGTCTGCAGAACTTTATTGGCA
M21850/-        AAGGAGTGGAAGAAGGTTCCATCGGGAAAGTGTGCAGGACCTTACTGGCG
AF156457/-      AGGGCGTGGAGGAAGGATCCATTGGAAAGGTCTGCAGGACTCTGTTGGCA
M26087/-        AAGGAGTGGAAGAAGGCTCAATCGGGAAAGTTTGCAGGACCTTGTTAGCA
M26088/-        AAGGAGTAGAAGAAGGTTCCATTGGGAAAGTATGCAGGACTCTGCTAGCA
AF222820/-      AGGGAGTGGAGGAAGGCTCCATCGGGAAGGTGTGCAGGACCTTACTAGCA


NC_002022/-     AAGTCGGTATTTAACAGCTTGTATGCATCTCCACAACTAGAAGGATTTTC
X17336/-        AAGTCGGTATTCAACAGCTTGTATGCATCTCCACAACTGGAAGGATTTTC
M21850/-        AAGTCTGTATTTAACAGCTTATATGCATCGCCACAACTTGAGGGATTTTC
AF156457/-      AAGTCTGTATTCAACAGCTTGTACGCATCTCCACAGCTGGAAGGGTTTCTC
M26087/-        AAATCTGTGTTTAACAGTTTATATGCATCTCCACAACTCGAAGGTTTTTC
M26088/-        AAGTCTGTATTCAACAGCTTGTATGCATCTCCACAACTTGAAGGTTTTTC
AF222820/-      AAGTCTGTGTTCAACAGCTTGTATGCATCTCCACAACTCGAGGGGTTTTC


NC_002022/-     AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAATC
X17336/-        AGCTGAATCAAGAAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAACC
M21850/-        AGCGGAATCTAGAAAACTGCTCCTCATTGTTCAGGCTCTTAGAGACAACC
AF156457/-      AGCTGAATCAAGGAAACTGCTTCTTATCGTTCAGGCTCTTAGGGACAACC
M26087/-        AGCTGAATCTAGGAAAATACTTCTCATTGTTCAGGCCCTTAGGGACAACC
M26088/-        AGCTGAGTCAAGAAAGCTGCTTCTCATTGTTCAGGCACTTAGGGACAACC
AF222820/-      AGCTGAATCAAGAAAACTGTTACTCATTGTTCAGGCACTTAGGGACAACC


NC_002022/-     TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
X17336/-        TGGAACCTGGGACCTTTGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
M21850/-        TGGAACCTGGAACCTTCGATCTTGGAGGGCTATATGGAGCAATTGAGGAG
AF156457/-      TGGAACCTGGAACCTTTGATCTTGGAGGATTGCATGAAGCAATTGAGGAG
M26087/-        TGGAACCTGGAACCTTTGATATTGGGGGGCTATATGAATCAATTGAGGAG
M26088/-        TGGAACCTGGCACCTTCGATCTTGGGGGGCTATATGAAGCAATTGAGGAG
AF222820/-      TGGAACCTGGAACCTTCGACATTGAAGGACTGTATGAAGCAATTGAGGAG


NC_002022/-     TGCCTAATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
X17336/-        TGCCTGCATTAATGATCCCTGGGTTTTGCTTAATGCTTCTTGGTTCAACTC
M21850/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF156457/-      TGCCTGATTAATGACCCCTGGGTTTTGCTTAATGCATCTTGGTTTAACTC
M26087/-        TGTCTGATTAATGATCCCTGGGTTTTGCTCAATGCATCTTGGTTCAACTC
M26088/-        TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC
AF222820/-      TGCCTGATTAATGATCCCTGGGTTTTGCTTAATGCATCTTGGTTCAACTC


NC_002022/-     GTTCCTTACACATGCATTGAGTTAGTTGTGGCAGTGCTACTATTTGCTAT
```

Figure 10

```
X17336/-      CTTCCTCACACATGCATTGAGATAGTTGTGGCAATGCTACTATTTGCTAT
M21850/-      CTTCCTCACACATGCAGTGAAATAGTTGTGGCAATGCTACTATTTGCTAT
AF156457/-    CTTCCTCACACATG------------------------------------
M26087/-      CTTCCTTACACATGCACTAAAGTAGTTGTGGCAATGCTACTATTTGCTAT
M26088/-      CTTCCTCACACATGCAGTGAAATAGTTGTGGCAATGCTACTATTTGCTAT
AF222820/-    C-------------------------------------------------


NC_002022/-   CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--   (SEQ ID NO: 127)
X17336/-      CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--   (SEQ ID NO: 128)
M21850/-      CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--   (SEQ ID NO: 129)
AF156457/-    -----------------------------------  (SEQ ID NO: 130)
M26087/-      CCATACTGTCCAAAAAAGTACCTTGTTTCTACT--   (SEQ ID NO: 131)
M26088/-      ACATCCTGTCCAAAAAAGTACCTTGTTTCTACT--   (SEQ ID NO: 132)
AF222820/-    -----------------------------------  (SEQ ID NO: 133)
```

PR8, MOI=0.01

Mock TF
GFP
PB1-2257
PB2-2040
PA-2087(G)
NP-231
NP-390
NP-1496

FIGURE 11A

WSN, MOI=0.01

Mock TF
GFP
PB1-2257
PB2-2040
PA-2087(G)
NP-231
NP-390
NP-1496
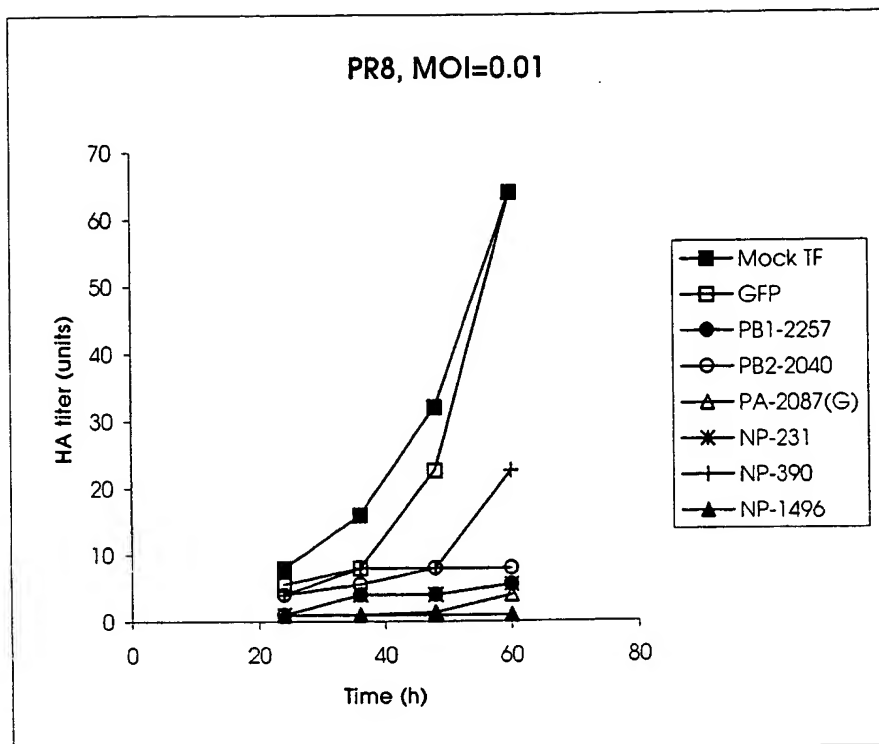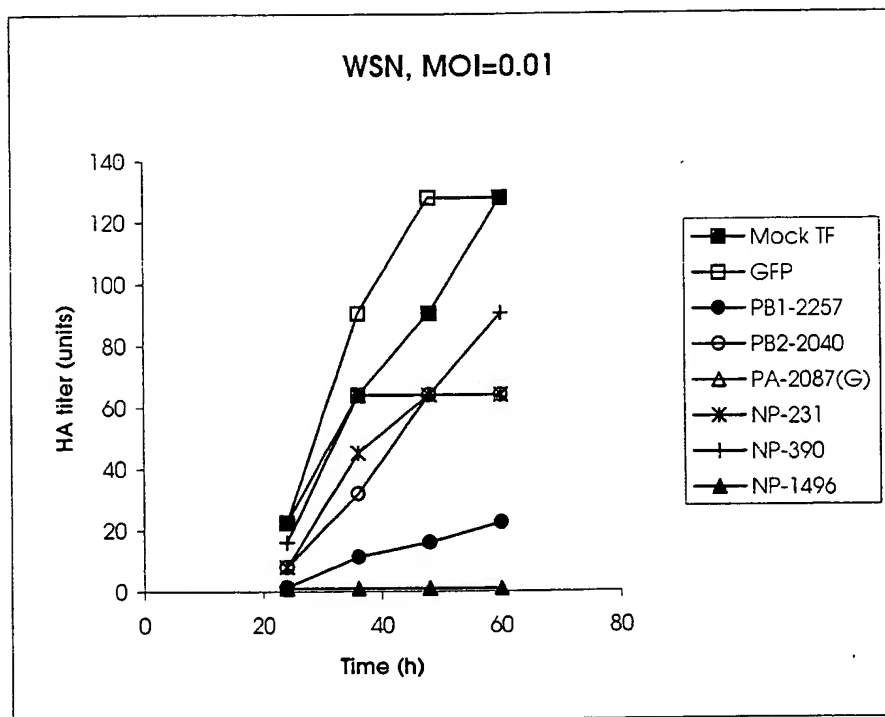
FIGURE 11B

Potent inhibition of influenza A viral replication by NP-1496 siRNA
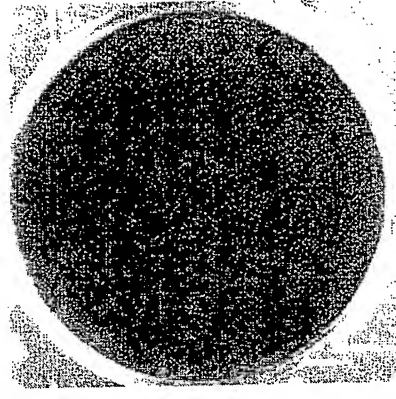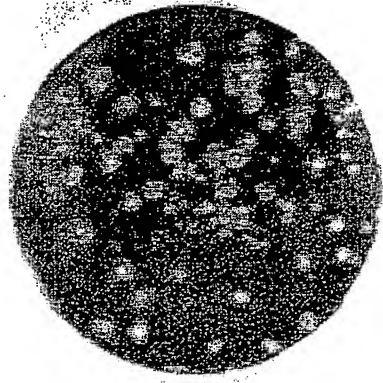
	Mock transfection	NP-1496 siRNA 2.5 nmole	Fold difference
MOI=0.001	6×10^5 PFU/ml	<20 PFU/ml	3×10^4
MOI=0.1	1×10^6 PFU/ml	5×10^3 PFU/ml	2×10^3
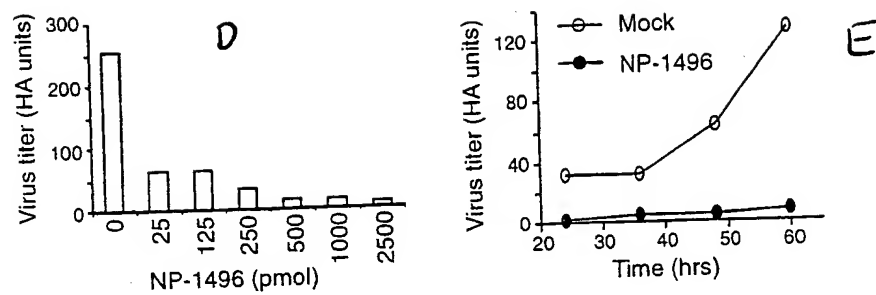
FIGURE 11C

Figure 11

Figure 12

```
PR8   (H1N1)       TCTCGGACGAAAAGGCAGCGAGCCCGATCGTGCCTTCCTTTGACATGAGT
WSN   (H1N1)       TCTCGGACGAAAAGGCAGCGAGCCCGATCGTGCCCTCCTTTGACATGAGT
Lenn. (H2N2)       TCTCGGACTAAAAGGCAACGAACCCCATCGTGCCCTCTTTTGACATGAGT
HK    (H3N2)       TCTCGGACGAAAAGGCAGCGAACCCGATCGTGCCCTCTTTTGACATGAGT
Memphis (H3N2)     TCTCAGACGAAAAGGCAACGAACCCGATCGTGCCCTCTTTTGACATGAGT
HK    (H5N1)       TCTCAGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT
Duck  (H10N7)      TCTCGGACGAAAAGGCGACGAACCCGATCGTGCCTTCCTTTGACATGAGT
Equine (H7N7)      TCTCGGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGC
Whale (H13N2)      TCTCAGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT
Chicken (H9N2)     TCTCGGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT
Swine (H4N6)       TCTCGGACGAAAAGGCAACGAACCCGATCGTGCCTTCCTTTGACATGAGT
```

```
PR8   (H1N1)       AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA     (SEQ ID
NO: 134)

WSN   (H1N1)       AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA     (SEQ ID
NO: 135)

Lenn. (H2N2)       AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA     (SEQ ID
NO: 136)

HK    (H3N2)       AATGAAGGATCTTATTTCTTCGGACACAATGCAGAGGAGTACGACAATTA     (SEQ ID
NO: 137)

Memphis (H3N2)     AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAGTACGACAATTA     (SEQ ID
NO: 138)

HK    (H5N1)       AATGAAGGATCTTATTTCTTCGGAGACAATGCAGAGGAATATGACAATTG     (SEQ ID
NO: 139)

Duck  (H10N7)      AACGAGGGATCTTATTTCTTCGGAGACAATGCAGAGGAATATGACAATTA     (SEQ ID
NO: 140)

Equine (H7N7)      AATGAAGGGTCTTATTTCTTCGGAGACAATGCTGAGGAGTTTGACAGTTA     (SEQ ID
NO: 141)

Whale (H13N2)      AATGAGCGATCTTATTTCTTCGGAGACAATGCTGAGGAGTATGACAATTG     (SEQ ID
NO: 142)

Chicken (H9N2)     AATGAAGGATCTTATTTCTTCGGACACAATGCATAGGAGTATGACAATTA     (SEQ ID
NO: 143)

Swine (H4N6)       AACGAAGGGTCTTATTTCTTCGGAGACAATGCAGAGGAATATGACAATTA     (SEQ ID
NO: 144)
```

Summary of the inhibition effect of siRNAs on influenza A virus production

FIGURE 13

Yolk sac

Albumin

Amniotic cavity

Allantoic cavity

Influenza virus

siRNA
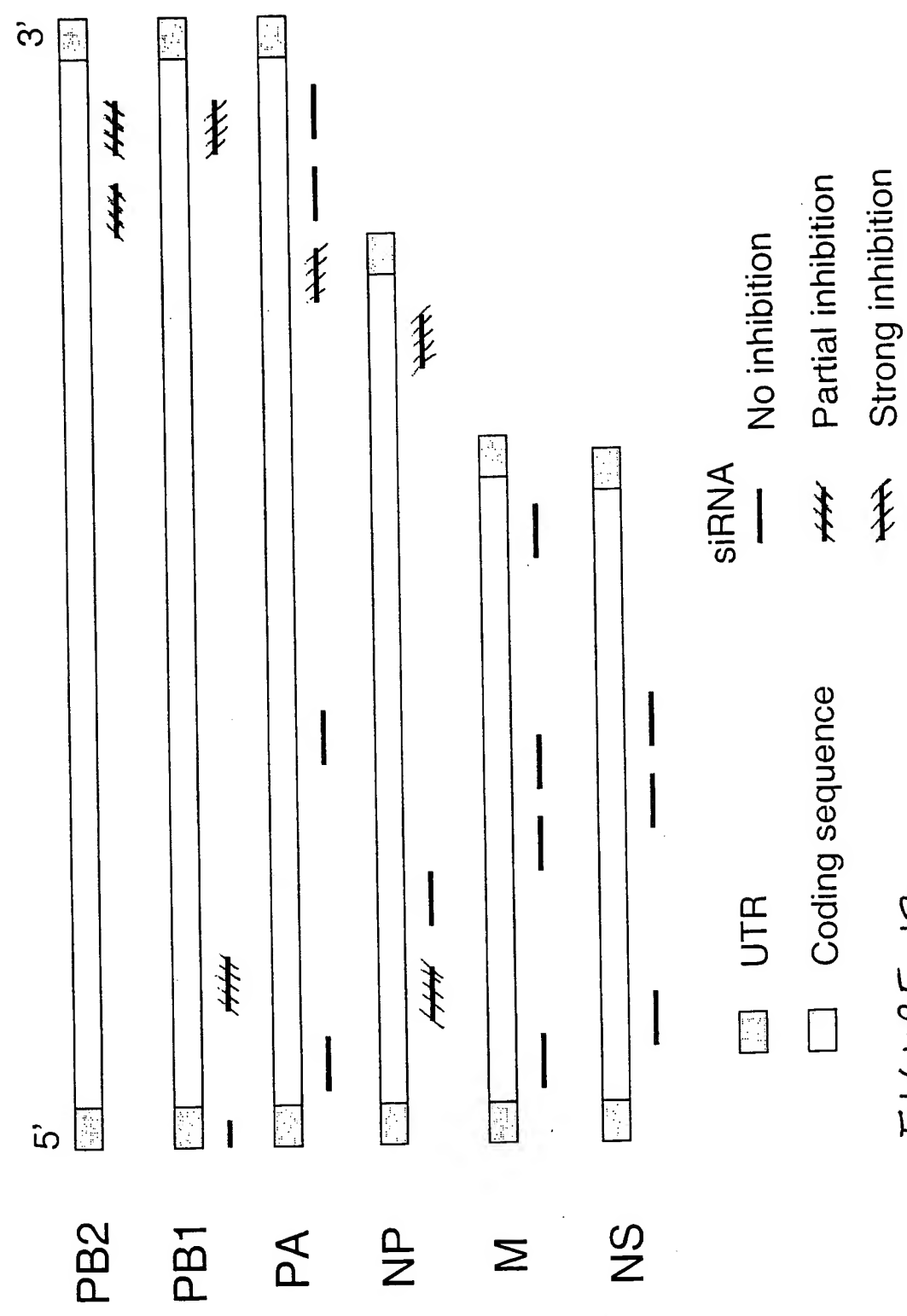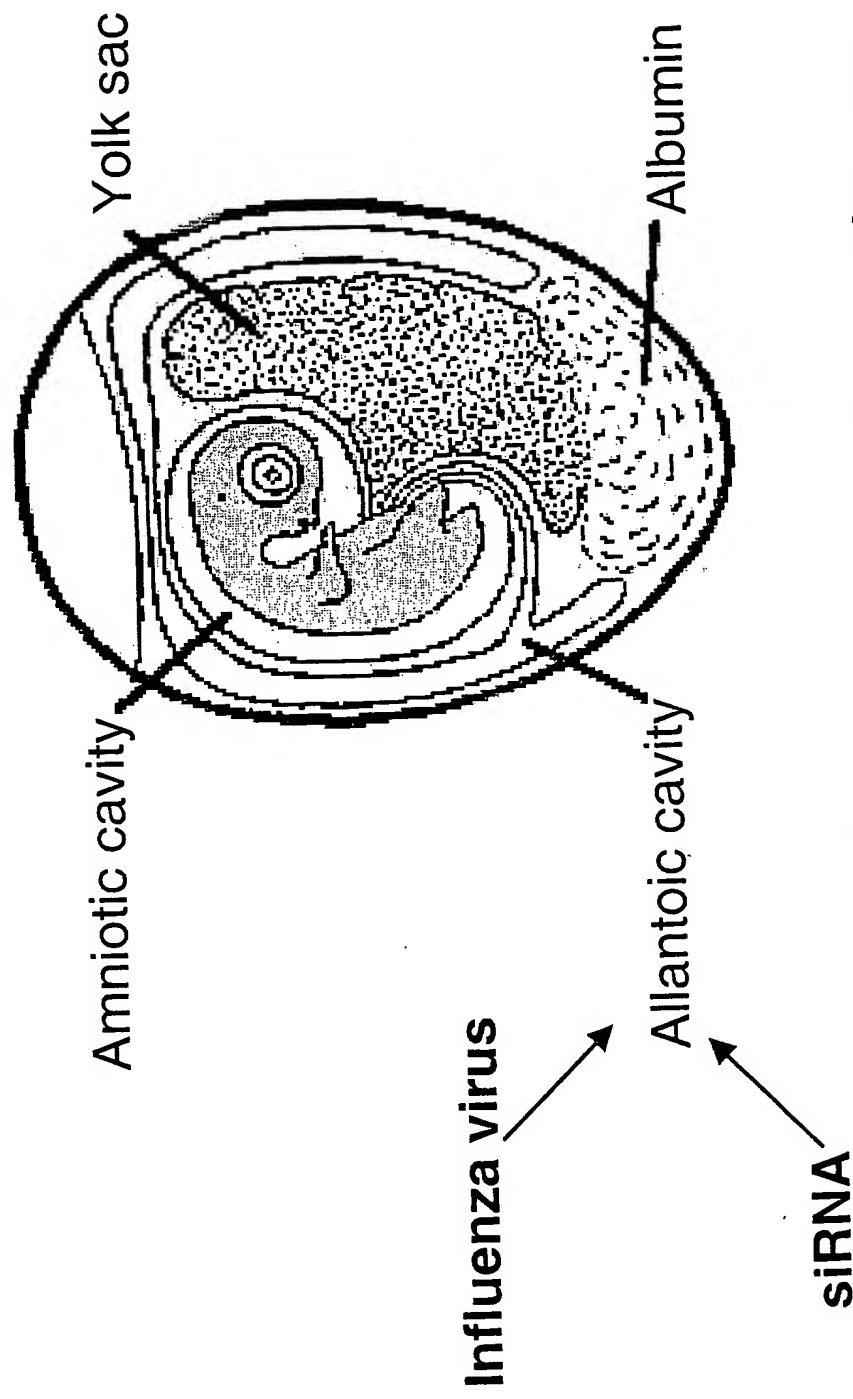
10-day old fertilized chicken egg

FIGURE 14A

The inhibition of influenza A virus replication in chicken embryos
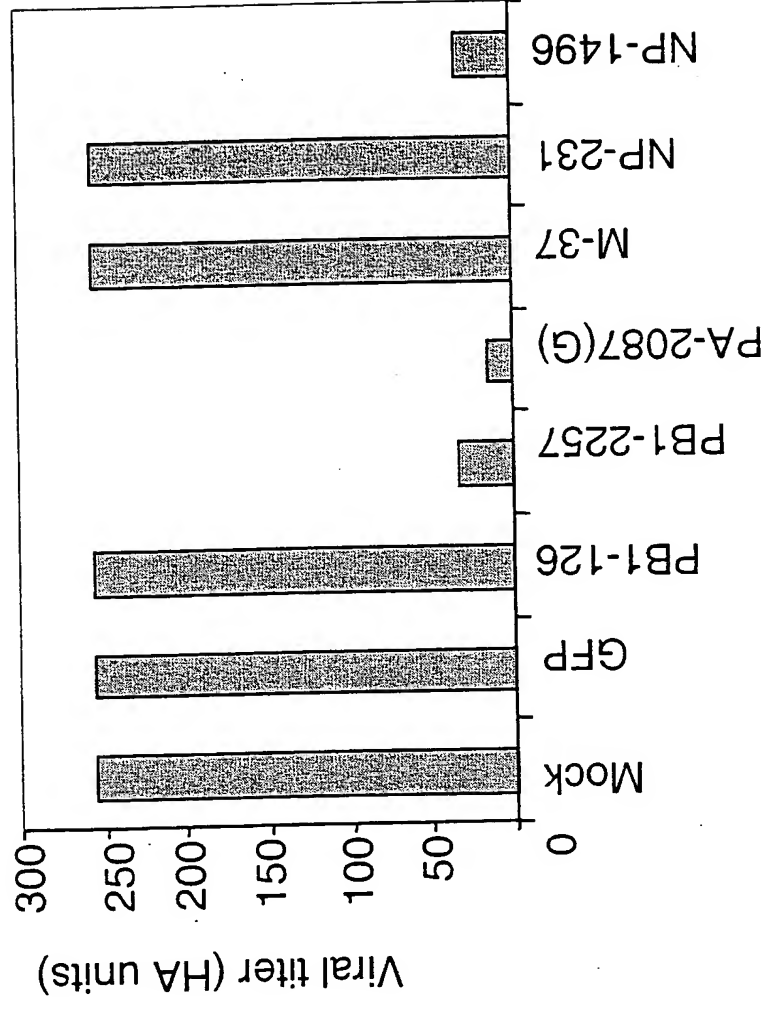
FIGURE 14B

Nucleocapsid protein

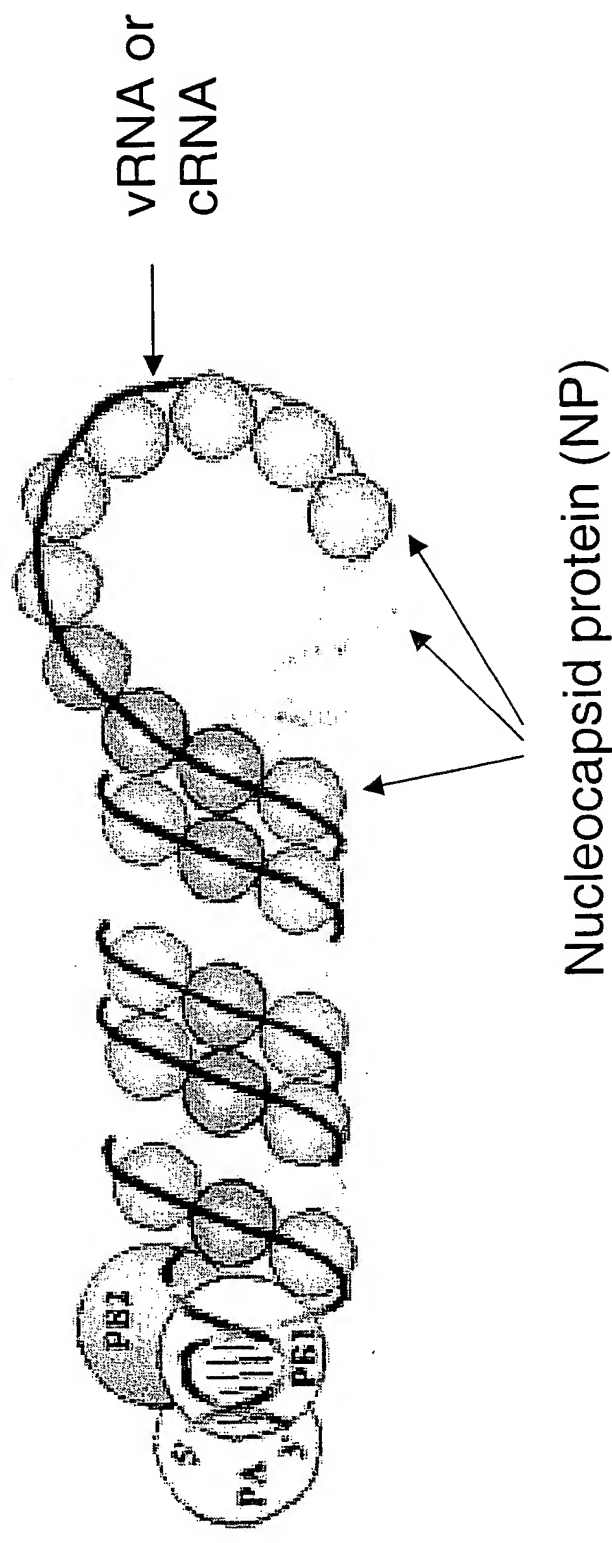## RNA-binding protein pivotal to virus replication

vRNA or cRNA
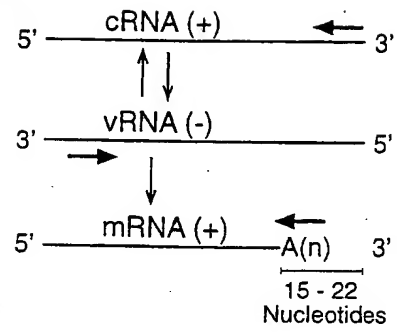
Nucleocapsid protein (NP)

Nucleocapsid protein

FIGURE 15

Figure 16A

Diagram of influenza virus virion RNA (vRNA), mRNA and full-length cRNA or template RNA

vRNA

3' UCGCUUCGUCC —————— GGAACAAAGAUGAppp 5'

U

SEQ ID NO: 146

SEQ ID NO: 145

mRNA

5' m^7GpppX^{m}Y······AGGCGAAAGCAGG —————— A$_{(n)}$ 3'

G A

10 - 13 Nucleotides

SEQ ID NO: 147

15 - 22 Nucleotides

template RNA

5' pppAGGCGAAAGCAGG —————— CCUUGUUUCUACU 3'

A

SEQ ID NO: 148

SEQ ID NO: 149
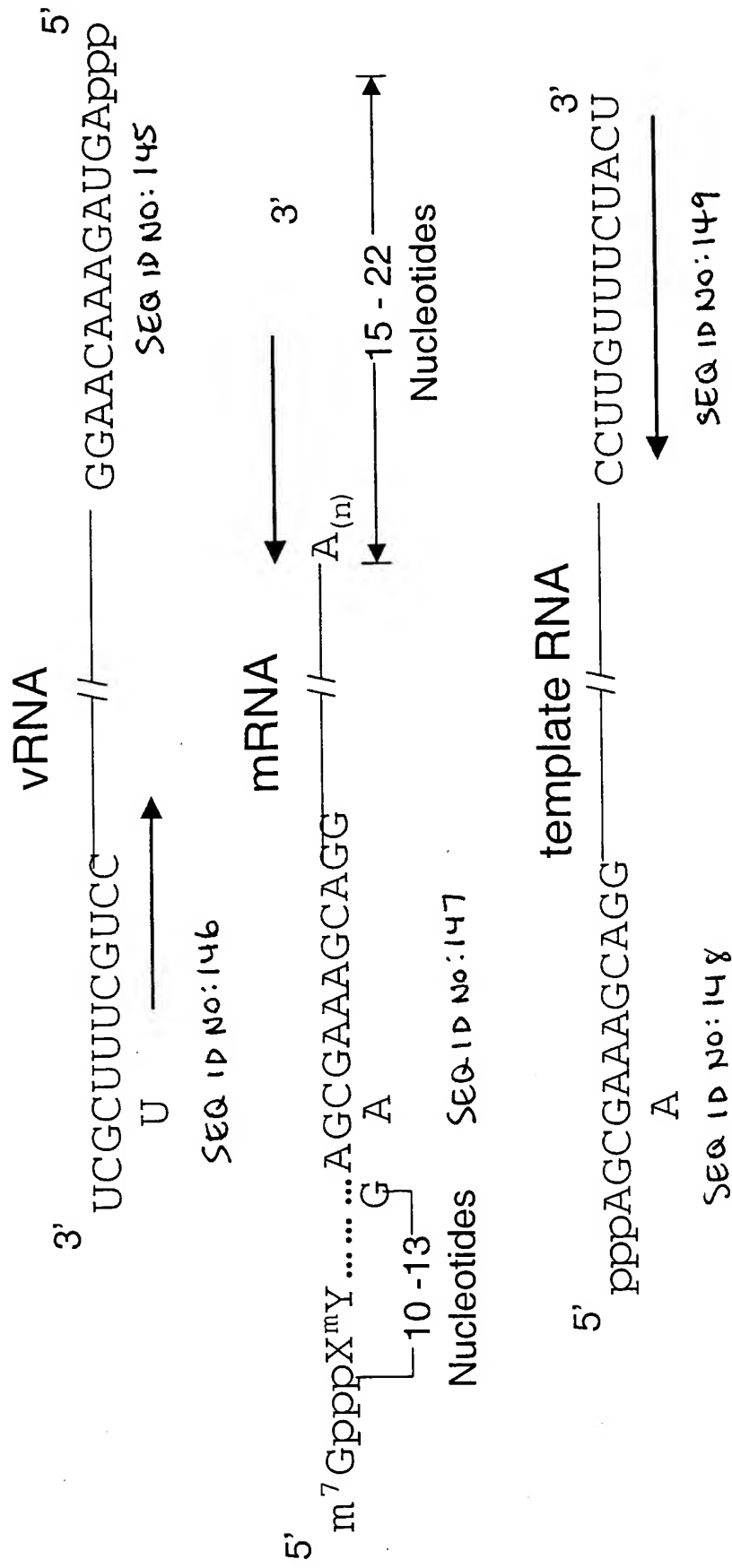
FIGURE 16B

NP siRNA interferes with virus replication at a very early stage
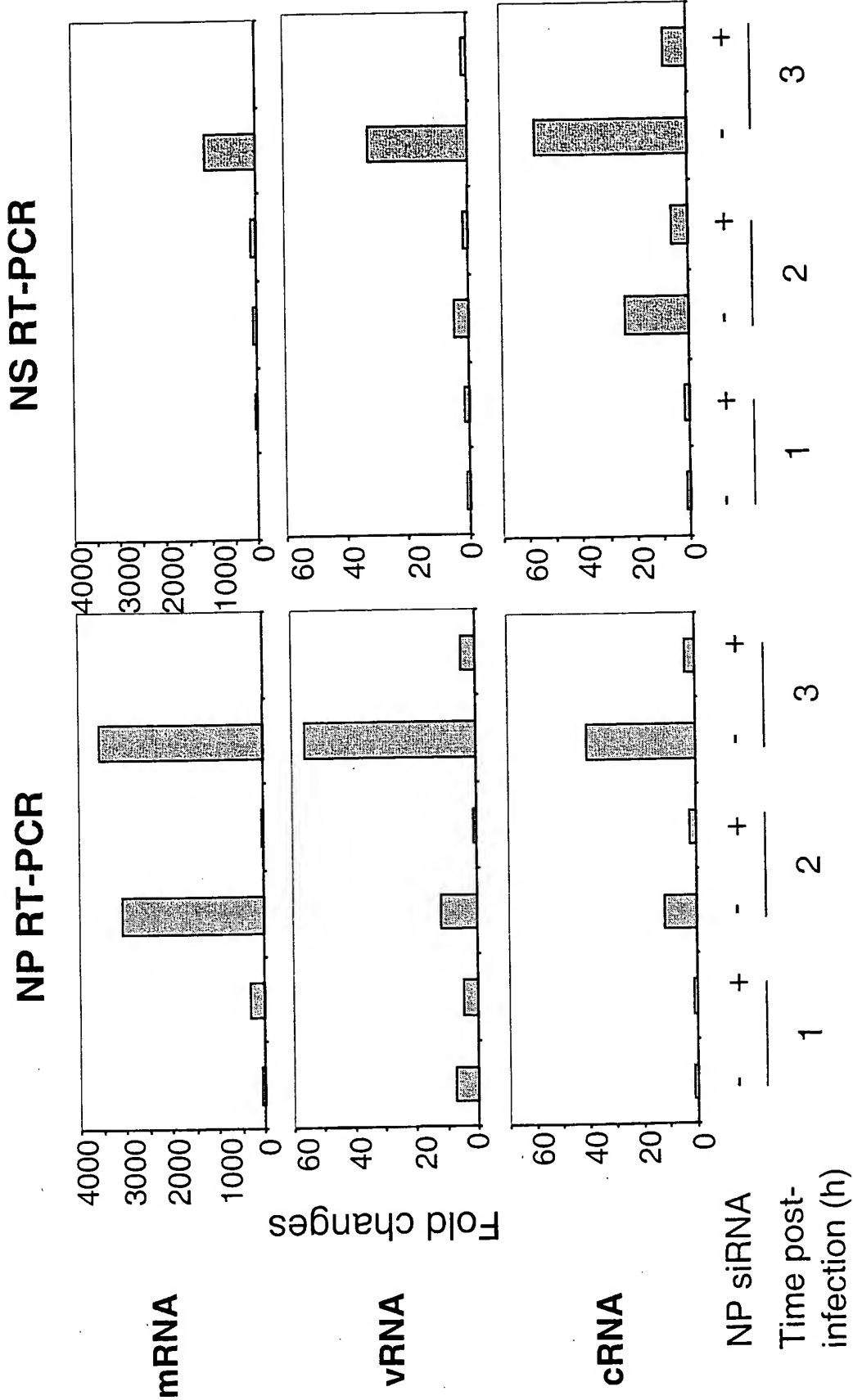
FIGURE 17
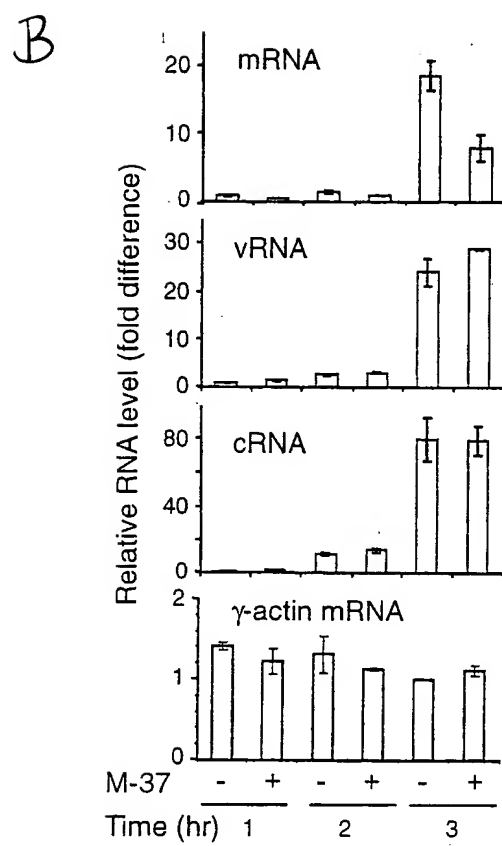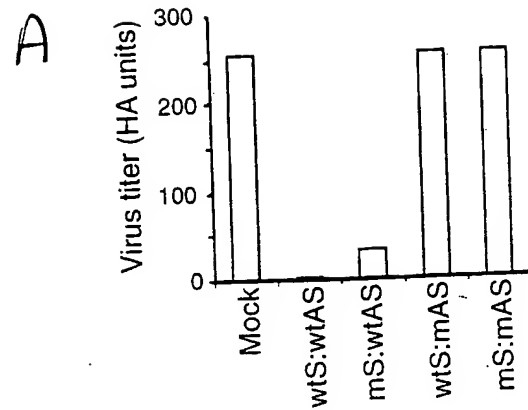
Figure 18
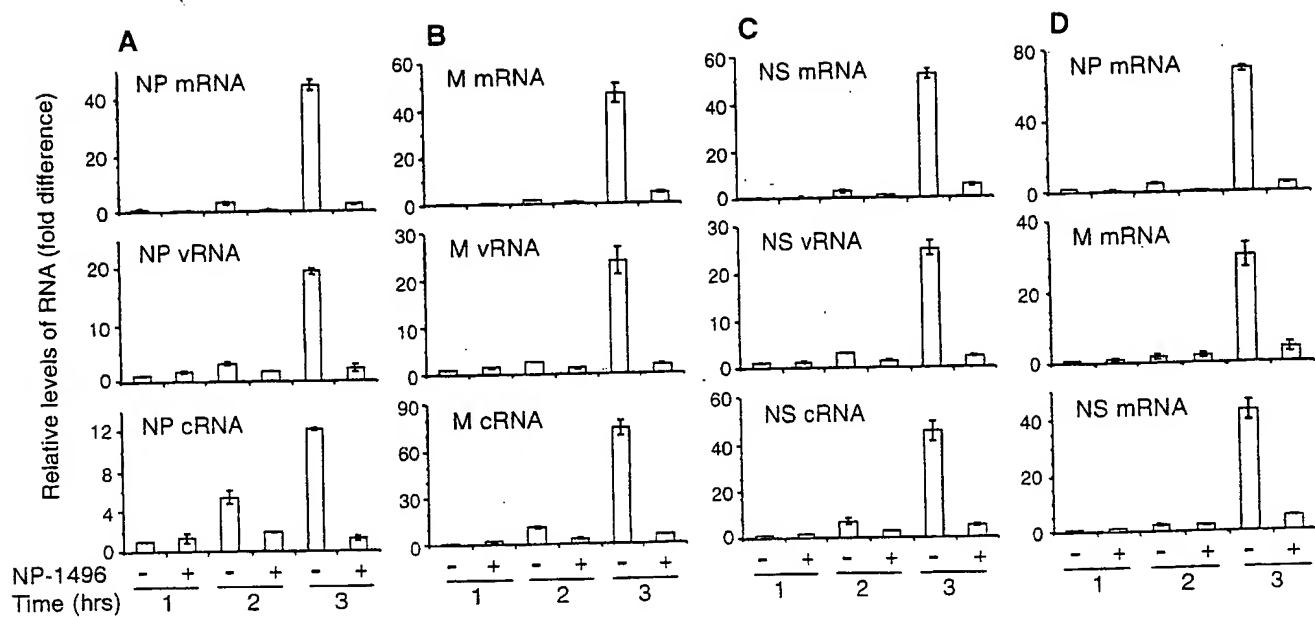
Figure 19A-D

NP and PA siRNA interferes with viral mRNA transcription
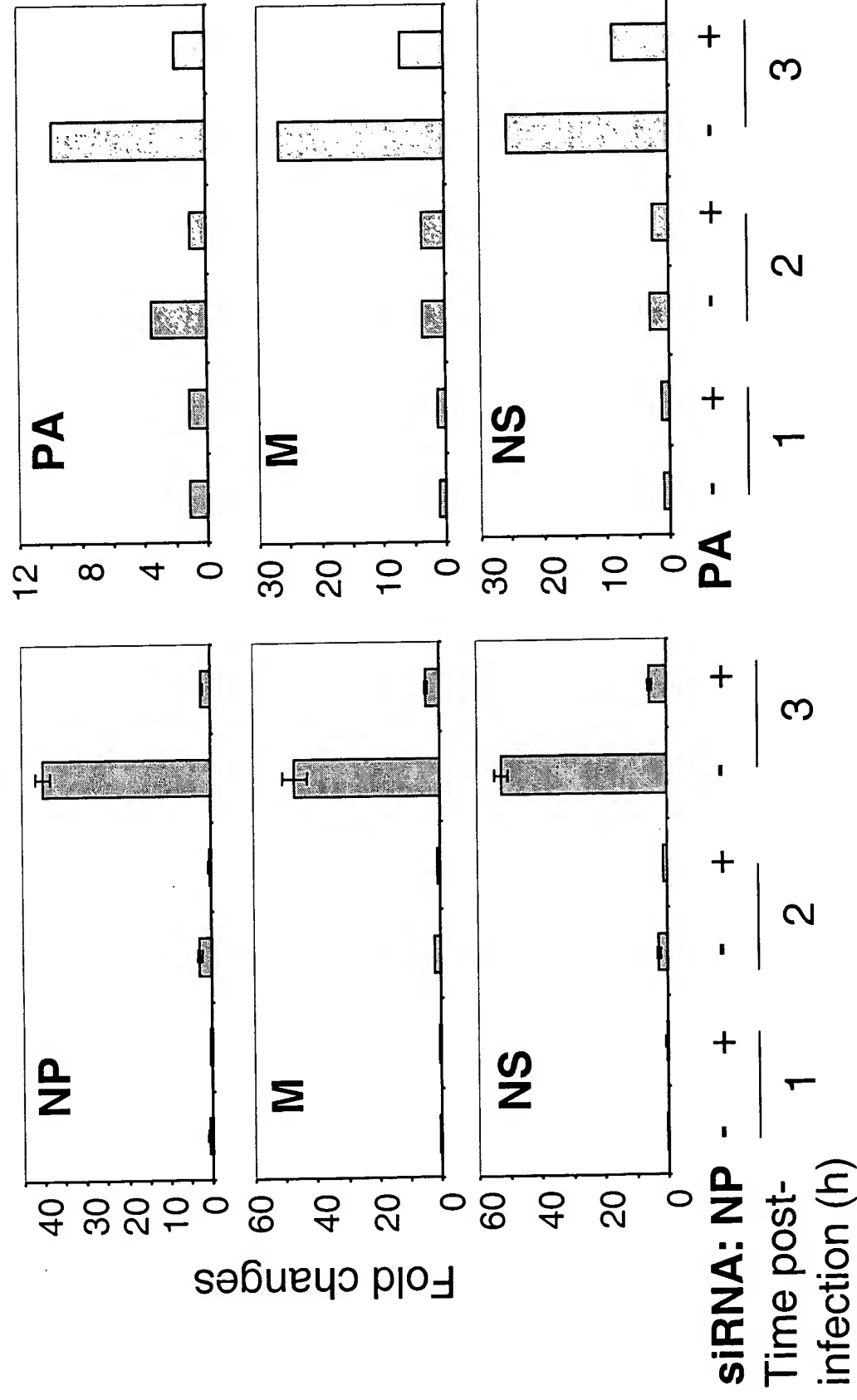
Figure 19E

NP and PA siRNA interferes with viral vRNA replication
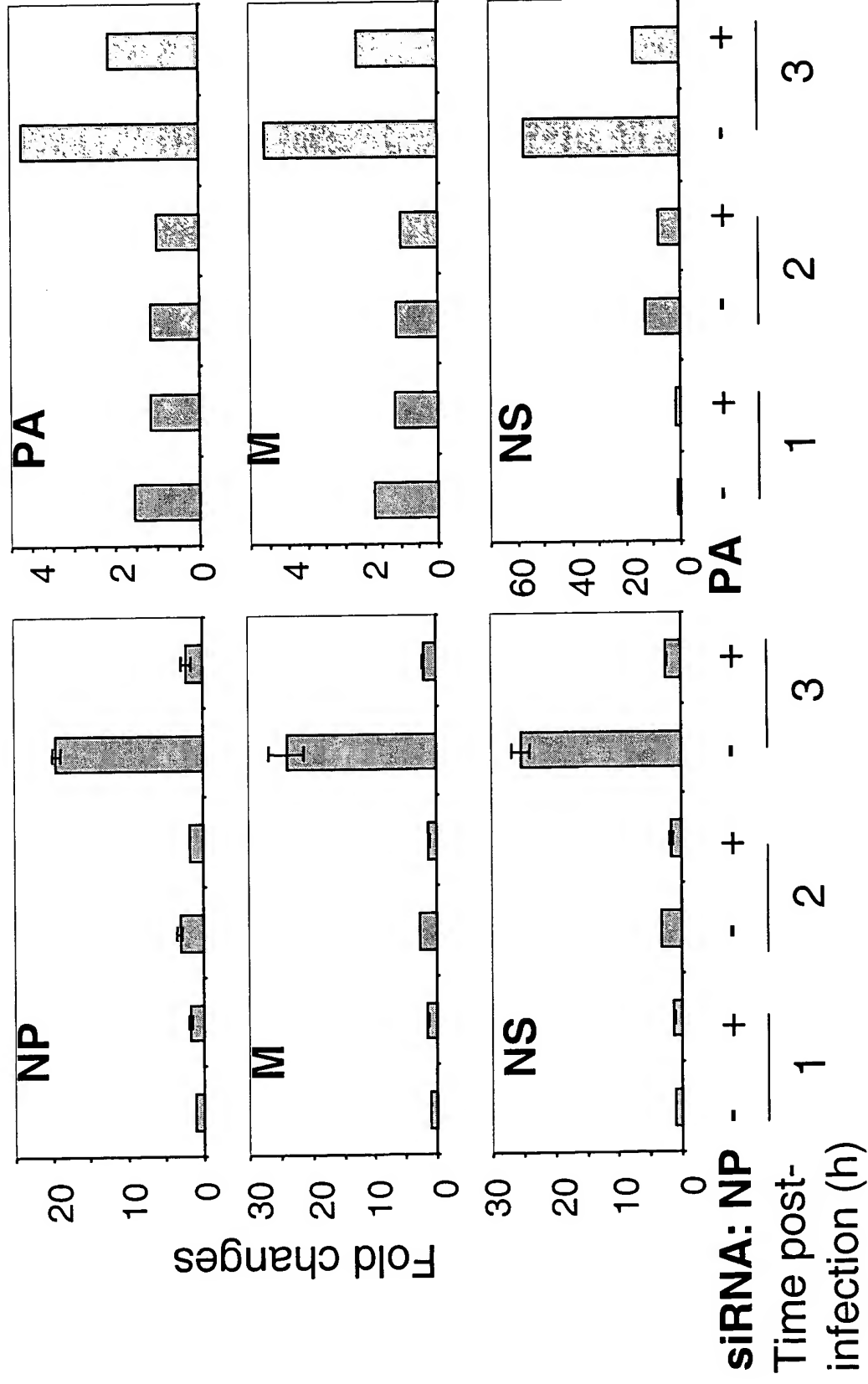
Figure 19F

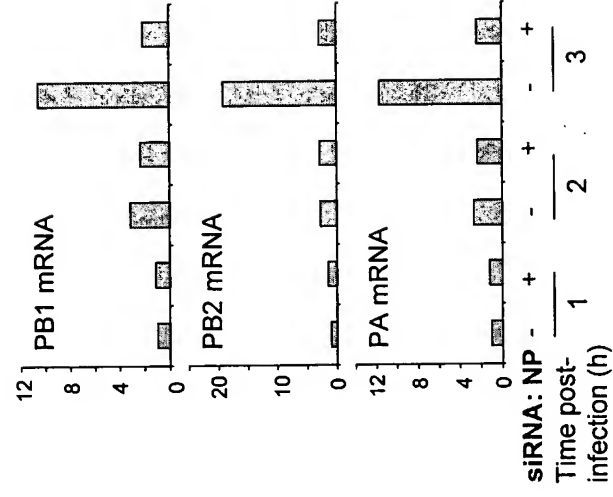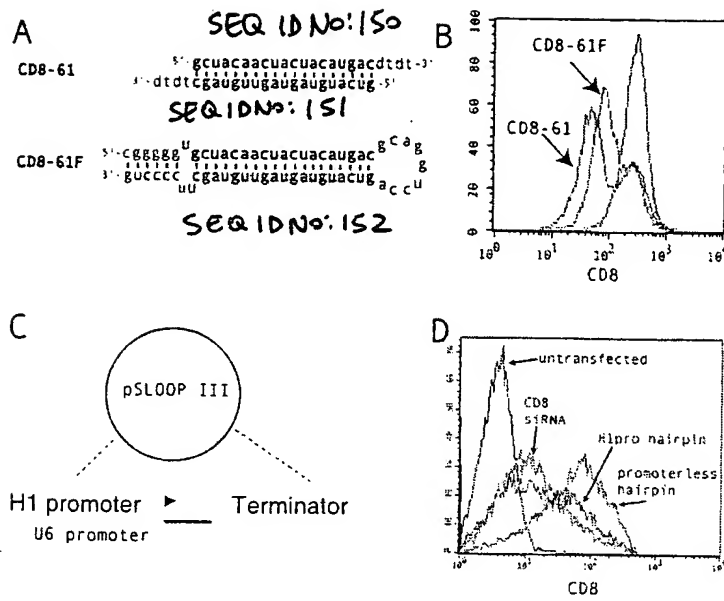# NP and PA siRNA interferes with viral cRNA replication

Figure 19 G

PB1 mRNA

PB2 mRNA

PA mRNA

siRNA: NP

Time post-
infection (h)

Figure 19 H

Figure 20

A

NP-1496

```
           ggaucuuauuucuucggagdtdt      SEQ ID NO: 153
           ||||||||||||||||||||||
        dtdtccuagaauaaagaagccuc         SEQ ID NO: 154
```

NP-1496H

```
               u                  c
        cggggg ggaucuuauuucuucggag g a g
        |||||  |||||||||||||||||||      g   SEQ ID NO: 155
        guccc  ccuagaauaaagaagccuc  a c u
              uu
```

GFP-949

```
           ugcgcuccuggacguagccdtdt      SEQ ID NO: 156
           ||||||||||||||||||||||
        dtdtacgcgaggaccugcaucgg         SEQ ID NO: 157
```

GFP-949H

```
               u                  c
        cggggg ugcgcuccuggacguagcc g a g
        |||||  |||||||||||||||||||      g   SEQ ID NO: 158
        guccc  acgcgaggaccugcaucgg  a c u
              uu
```

B

NP-1496H   GFP-949H

```
       u                  c         u                  c
cggggg ggaucuuauuucuucggag g a g cggggg ugcgcuccuggacguagcc g a g
|||||  |||||||||||||||||||     g |||||  |||||||||||||||||||     g   SEQ ID NO: 159
guccc  ccuagaauaaagaagccuc a c u guccc  acgcgaggaccugcaucgg a c u
      uu                               uu
```

GFP-949H   NP-1496H

```
       u                  c         u                  c
cggggg ugcgcuccuggacguagcc g a g cggggg ggaucuuauuucuucggag g a g
|||||  |||||||||||||||||||     g |||||  |||||||||||||||||||     g   SEQ ID NO: 160
guccc  acgcgaggaccugcaucgg a c u guccc  ccuagaauaaagaagccuc a c u
      uu                               uu
```

C

Figure 21

siRNA prevent influenza virus production in mice

Log₁₀ TCID 50

P=0.0002

(average)

	NT	GFP	NP	NP
	10⁴·²	10⁴·²	10³·⁹	10³·²
			30 μg	60 μg
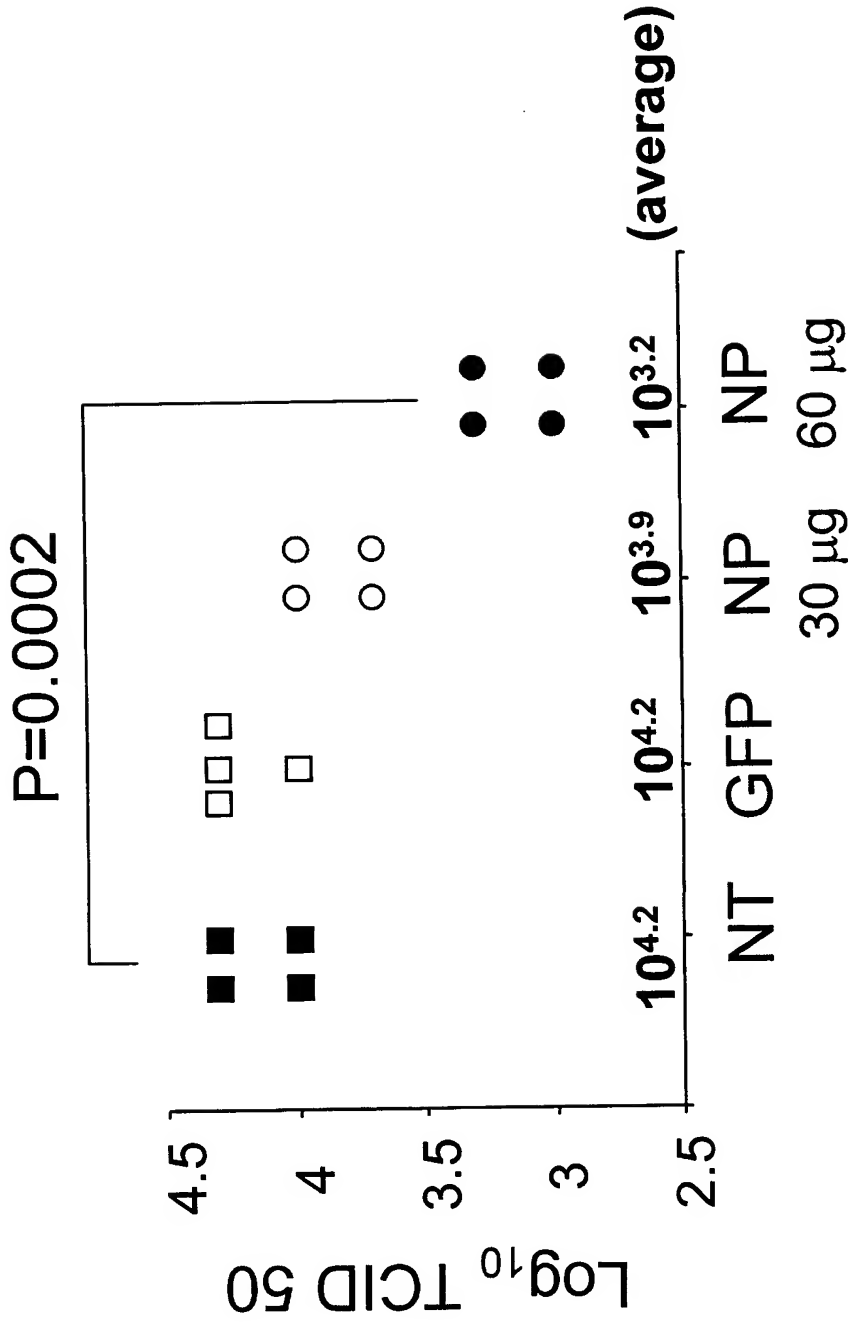
siRNA + →3 h PR8, →24 h 25 μl lung →MDCK
Carrier 1, i.v. 2k pfu/mouse homogenate HA assay

FIGURE 22 A

The in vivo Transfection Effect of Poly–L–Lysine(42K)
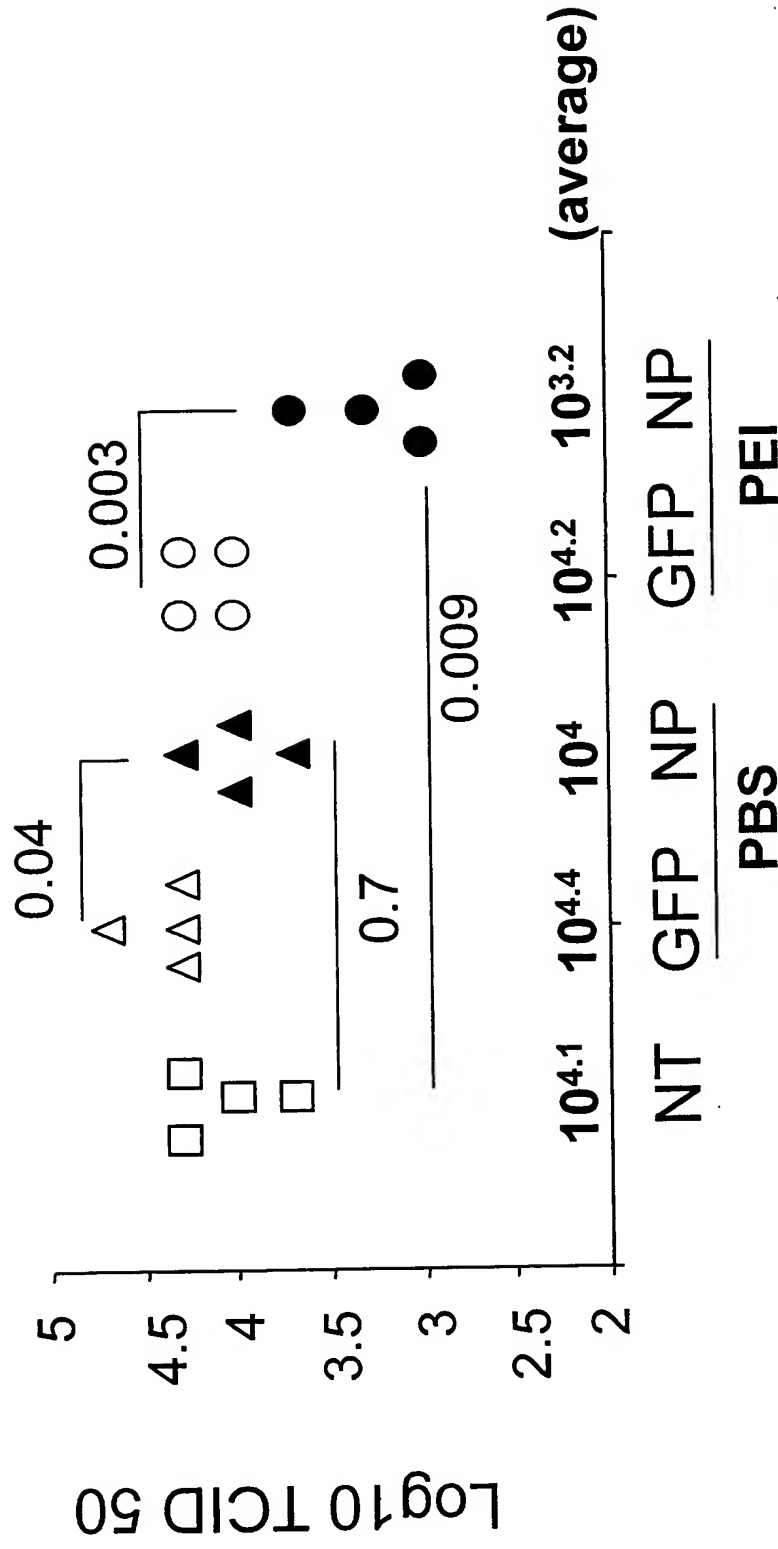

FIGURE 22B

siRNA Prevent Influenza Virus Production in vivo

FIGURE 22C

Additive/synergistic effect of siRNA against influenza virus in mice
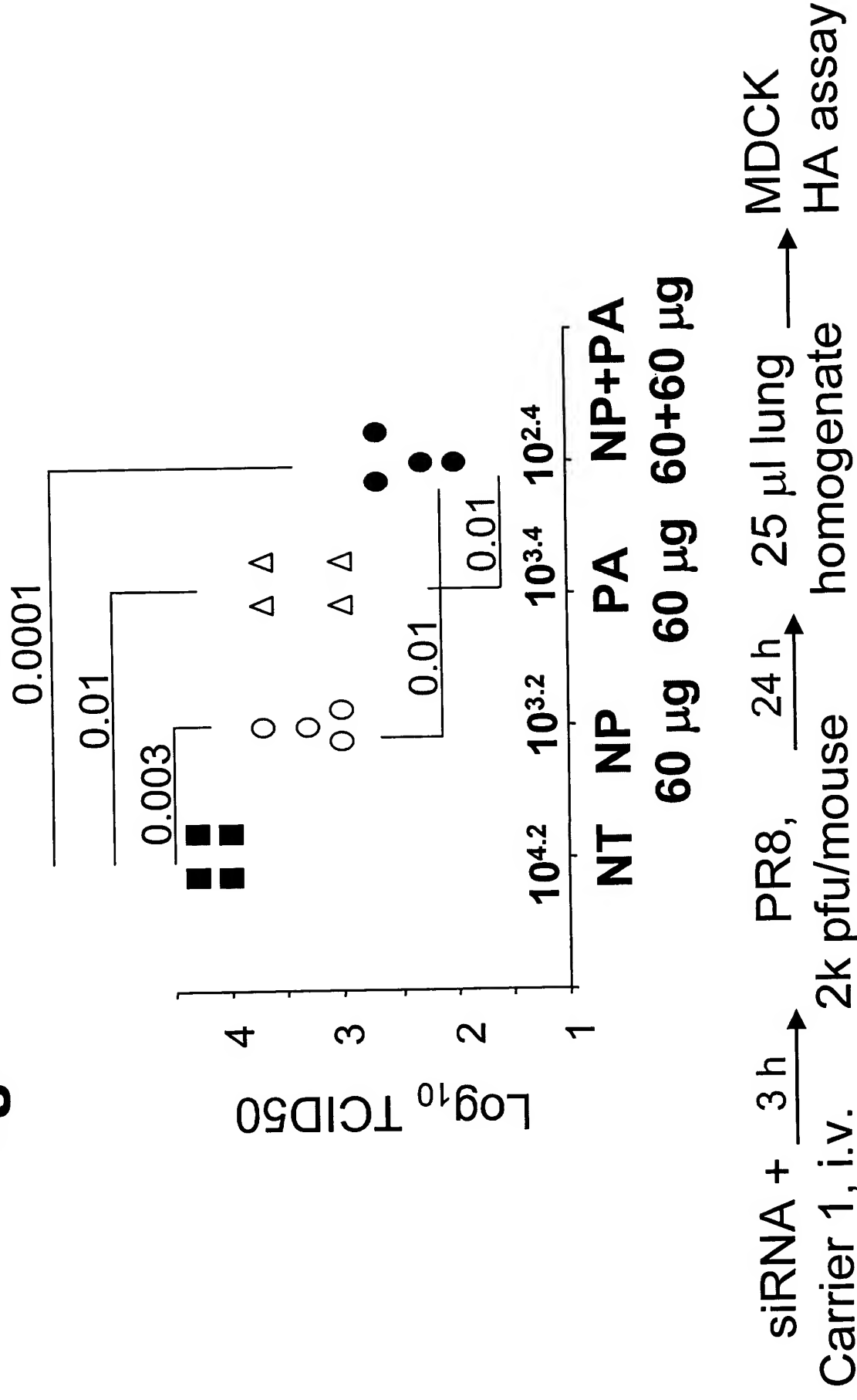
FIGURE 23

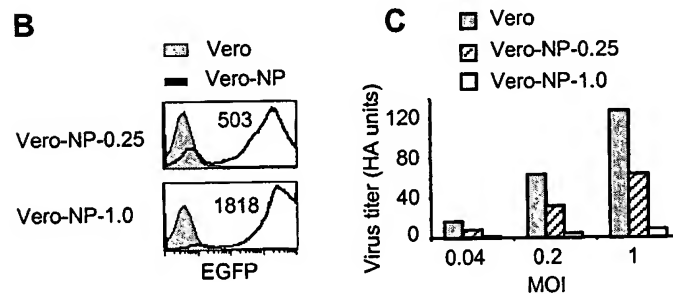# siRNA inhibit influenza virus Production in infected mouse
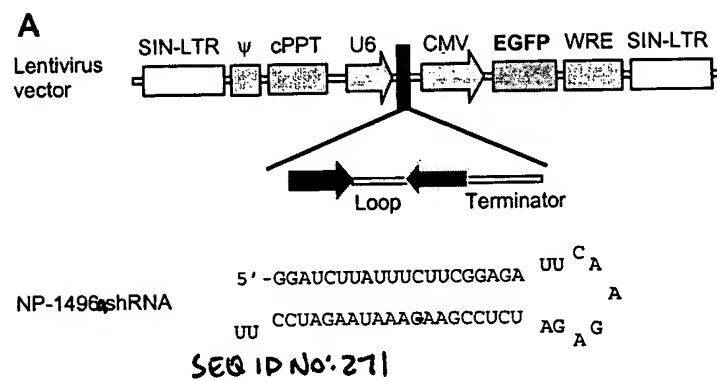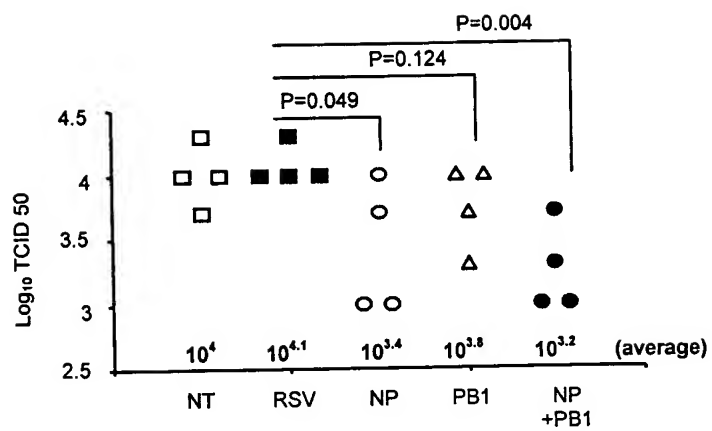

FIGURE 24

PR8,
500 pfu/mouse

A
Lentivirus vector

SIN-LTR Ψ cPPT U6 CMV **EGFP** WRE SIN-LTR

Loop Terminator

NP-1496 shRNA

5'-GGAUCUUAUUUCUUCGGAGA UU ^{C}A
                                      A
UU CCUAGAAUAAAGAAGCCUCU AG $_A$G

SEQ ID NO: 271

B

Vero
Vero-NP

Vero-NP-0.25   503

Vero-NP-1.0   1818

EGFP

C

Vero
Vero-NP-0.25
Vero-NP-1.0

Virus titer (HA units)

120
80
40
0

0.04   0.2   1
MOI
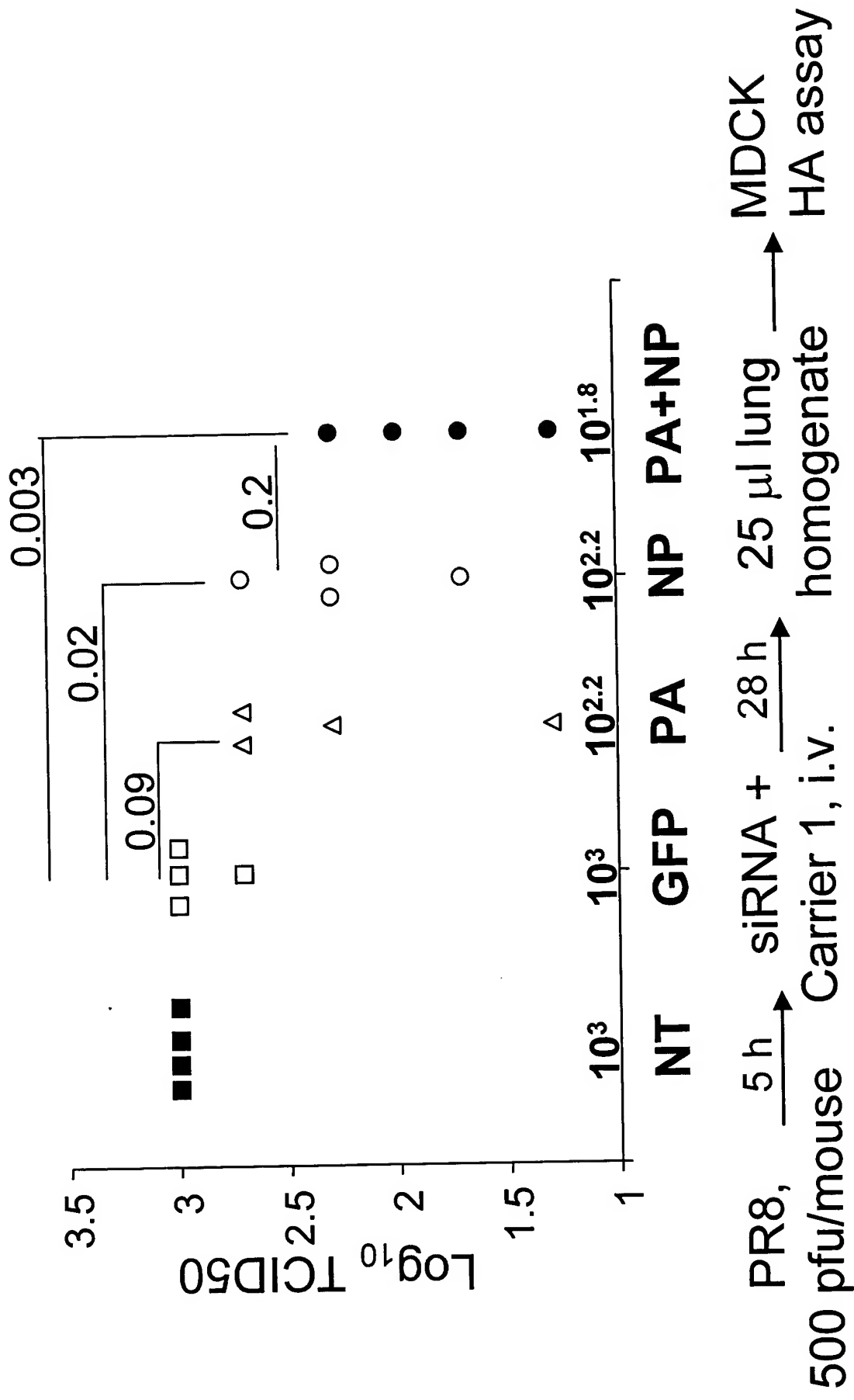
FIGURE 25

FIGURE 26
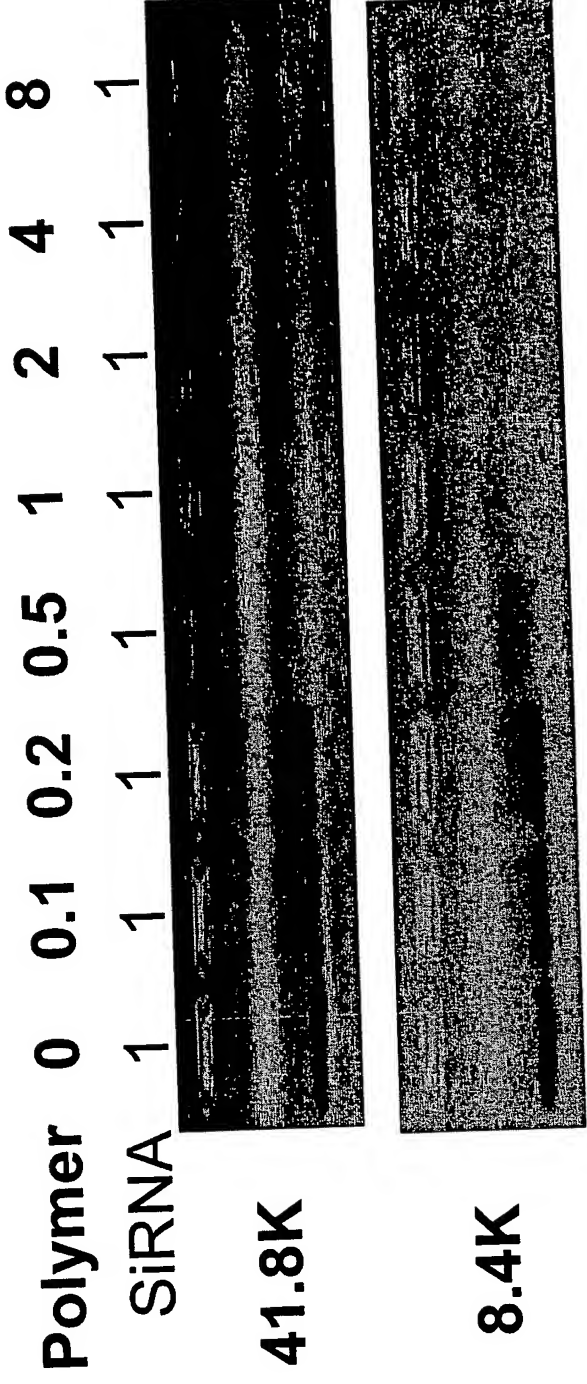
Electrophoretic retardation of siRNA with poly-L-lysine

Polymer	0	0.1	0.2	0.5	1	2	4	8
SiRNA	1	1	1	1	1	1	1	1

41.8K

8.4K

FIGURE 27A

Electrophoretic retardation of siRNA
with poly-L-arginine

PLA	0	0.02	0.06	0.17	0.5	1.5	4.5	13.5	43.5
SiRNA	1	1	1	1	1	1	1	1	1
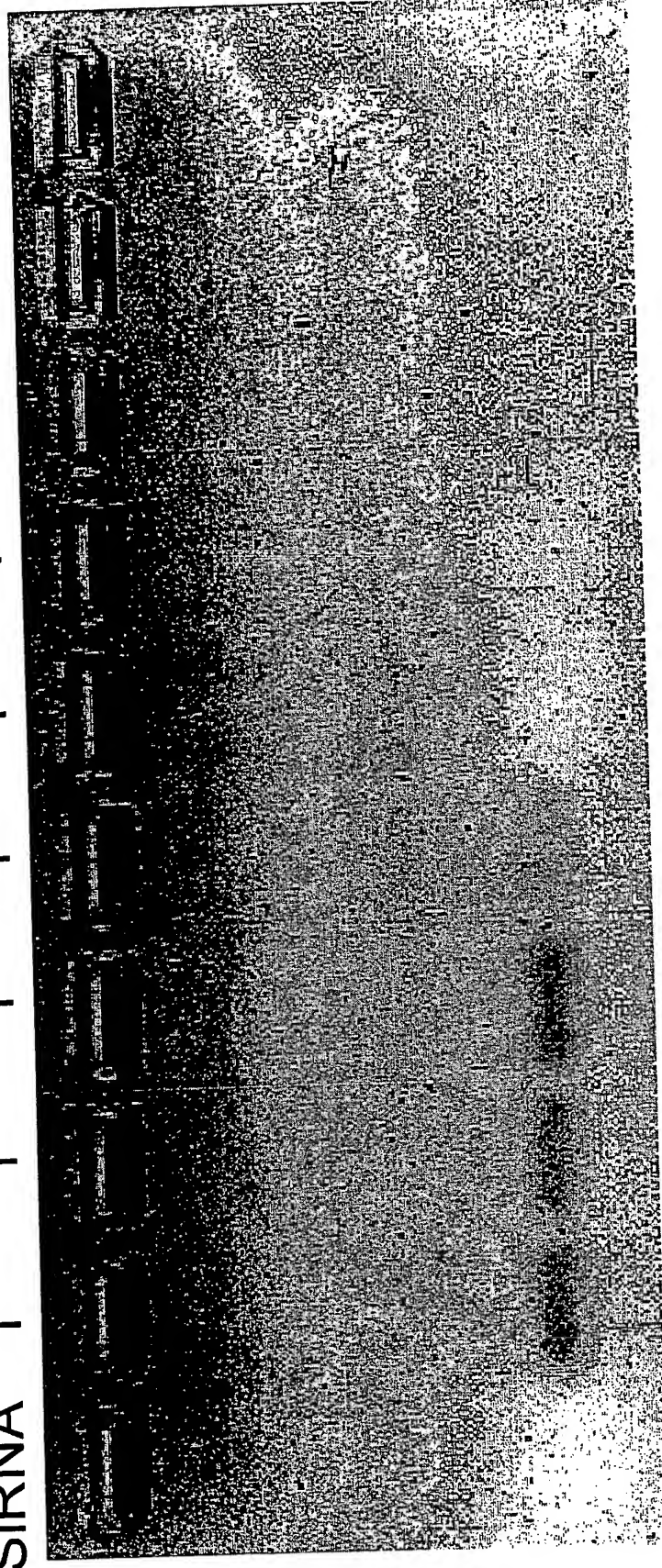
FIGURE 27B

Comparison of poly-L-lysine with different molecular weight

PLL:siRNA ratio

PLL42k
PLL8k

Percent relative viability
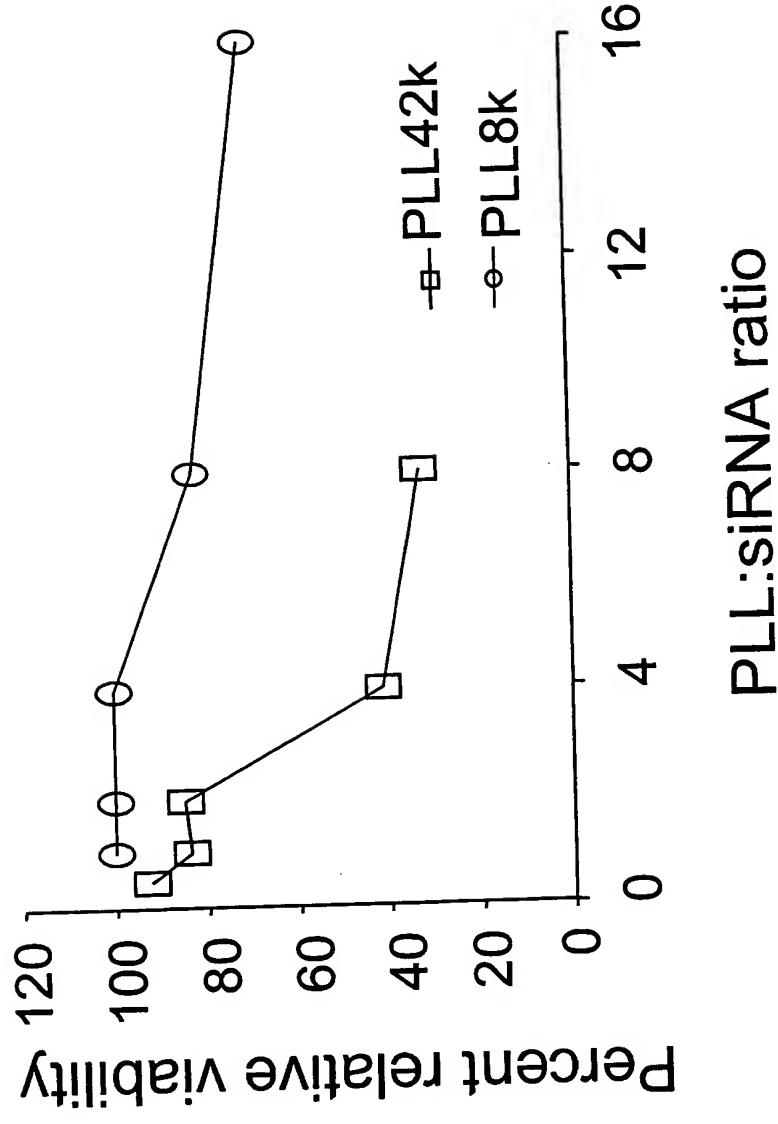
FIGURE 28A

In vitro cytotoxicity of poly-L-arginine
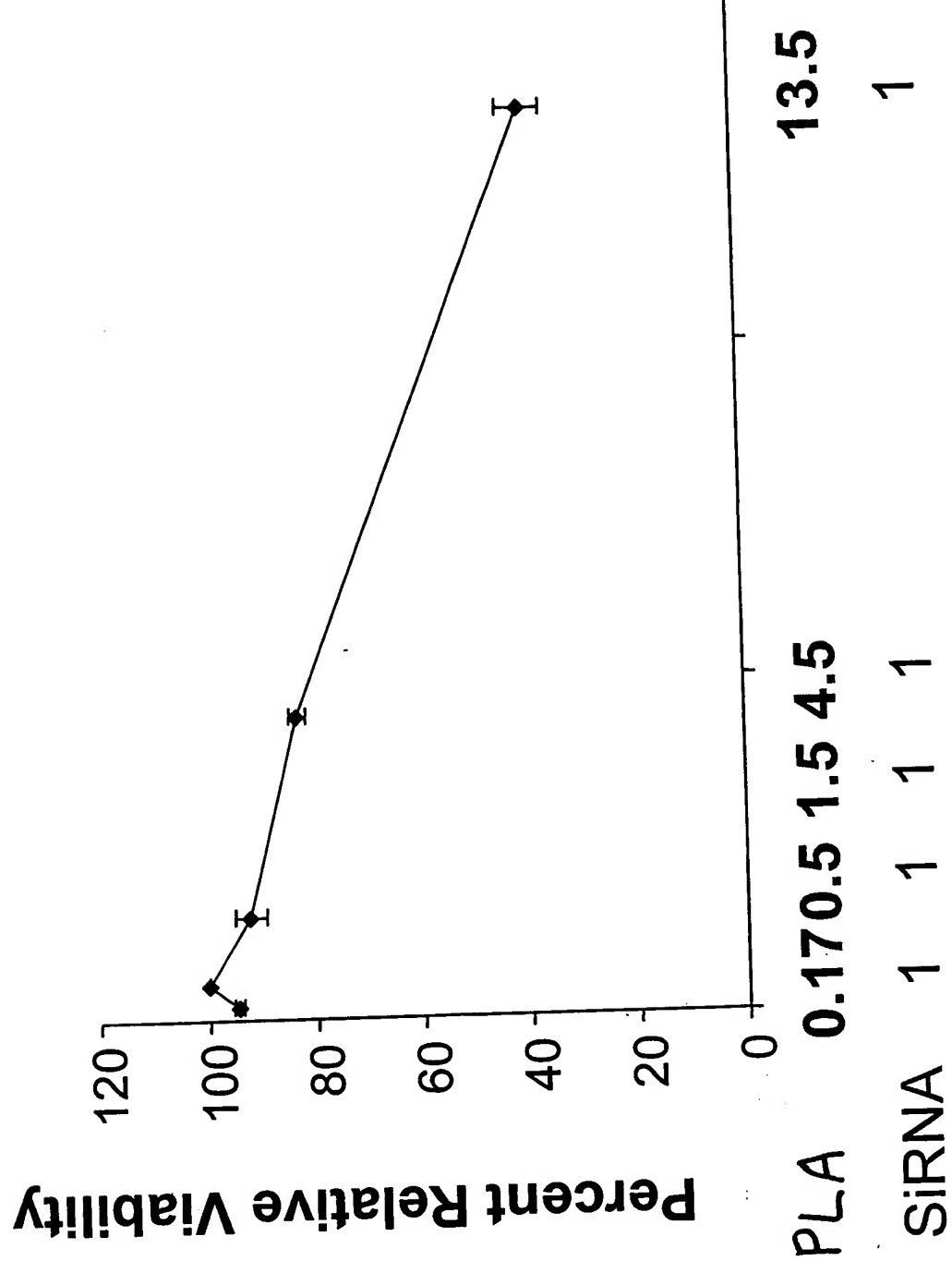
FIGURE 28B

Comparison of poly-L-lysine with different molecular weight

Viral titer (HA units)

Time post-infection (h)

NT
LF2k
42K,2:1
8K,8:1
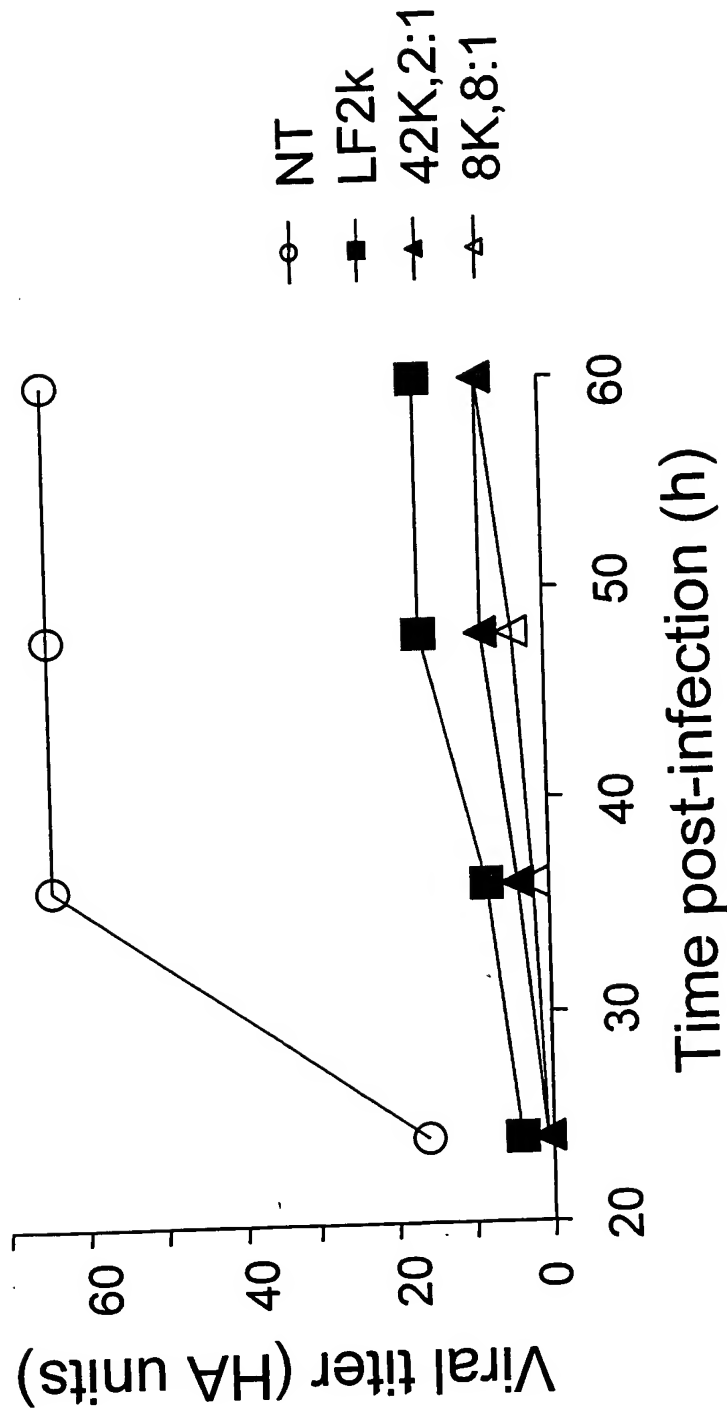
siRNA: 4×10^{-10} M

42K PLL: 2.9×10^{-10} M

8.4K PLL: 57×10^{-10} M

FIGURE 29A

Poly-L-arginine helps cellular uptake of siRNA in vitro

Virus titer (HA units) vs **Time post-infection (hrs)**

Legend:
- Mock
- LF2K
- 1:1(Rn:siRNA)
- 2:1
- 4:1
- 8:1

FIGURE 29B